Where Are We With Personalized Medicine: What’s Available Now & What Is On The Horizon?
Agenda

I. Overview Of Personalized Medicine

II. Personalized Medicine & The Future
   ◦ Bill W. Massey, Ph.D., Co-Founder & Chief Scientific Officer, MyGenesRX
   ◦ Tim Ramsey, Vice President, New Product Development, SureGene, LLC
   ◦ Nancy Grden, General Manager, Genomind, LLC
   ◦ Ben Weinstein, M.D., Director, Assessment Division, The Menninger Clinic

III. Questions & Discussion
Overview Of Personalized Medicine
Personalized Medicine

- Genomic medicine and personalized medicine utilize genetic information to prevent or treat disease.
- The physician develops a profile of the patient’s genetic distinction, or mapping.
- By investigating this genetic mapping, medical professionals are then able to profile patients, and use the information to plan out a course of treatment.
Personalized Medicine Compared With Traditional Medicine

Traditional “One-Size-Fits-All” Approach
All patients with the same diagnosis receive same treatment

Personalized Medicine Approach
Treatment strategy based on patient’s unique genetic profile

Genetic Profile A: Targeted Therapy
Genetic Profile B: Standard Therapy
Personalized Medicine: The Benefits & Challenges

**Benefits**
- Shift the emphasis in treatment from reaction to prevention
- Predict susceptibility to disease, improve disease detection, preempt disease progression
- Allows physicians to prescribe more effective drugs
- Eliminate trial-and-error inefficiencies that inflate health care costs and undermine patient care

**Challenges**
- Lack of standard regulatory requirements
- Lack of insurance reimbursement
- Incomplete legal protections to prevent genetic discrimination
- No medical education system to teach physicians how to incorporate personalized medicine into treatment
Personalized Medicine & The Future
Faculty

- Bill W. Massey, Ph.D., Co-Founder & Chief Scientific Officer, MyGenesRX
- Tim Ramsey, Vice President, New Product Development, SureGene, LLC
- Nancy Grden, General Manager, Genomind, LLC
- Ben Weinstein, M.D., Director, Assessment Division, The Menninger Clinic
Single Nucleotide Polymorphism (SNP)
What is personalized medicine?

• **Personalized medicine** - the use of primarily *genomic-based analysis* to direct a *therapeutic decision prior to treatment* that is particularly suited to the *individual patient*. The decision may include choice of medication, selection of dose, initiation of a preventative measure, or other therapeutic interventions.

• **Selecting the right drug for the right patient**
Patients respond differently to medications, thus requiring personalized treatment.

- Good Responders to Drug A
- Treatment Resistant or Refractory Patients
- Good Responders to Drug B
- Good Responders to Drug C
- Same Diagnosis, Different Prescription

PGx Testing
What pharmacogenomic tools are currently available to healthcare professionals?

• Genetic tests predictive of drug response
  – Genetic markers that indicate an innate propensity to response related to the drug’s mechanism of action (response markers)
  – Genetic markers that indicate an alteration in the innate ability to metabolize particular drugs via particular metabolic enzymes (metabolic markers) resulting in altered pharmacokinetics
WHAT IS SULT4A1?

Sulfotransferase family 4A, member 1 is a brain sulfotransferase with many interesting properties. However, its exact activities and mechanisms remain unknown.

• Highly expressed in areas thought to be involved in etiology of psychosis

• Highly conserve through-out evolution
  – Minimal difference between mouse and man
  – No coding variants in man, just regulatory variation

• Binds numerous classes of molecules that might impact psychosis
  – Catecholamines – norepinephrine, epinephrine, isoprenolene (but not dopamine)
  – Neurosteroids
  – Thyroid hormones
SULT4A1-1 status impacted response to olanzapine in the multiple studies, including CATIE.

Percentage of SUL4A1-1 positive and negative Caucasian patients that achieved clinically significant response in Phase I of the CATIE Study.
SULT4A1-1 Status-Appropriate Olanzapine Use Negates Olanzapine Weight Gain

SULT4A1-1 negative but not SULT4A1-1 positive patients treated with olanzapine gained more weight than subjects treated with other atypical antipsychotics.
1 in 5 schizophrenia patients will be hospitalized in a given year.

1 in 2 hospitalized patients will return to the hospital within a year.
Treating SULT4A1-1 positive Caucasian patients with olanzapine or quetiapine reduced the risk of hospitalization by over 80% in the CATIE Study.
Serotonin Transporter Response Marker

Genetic variation in the serotonin transporter gene (SLC6A4) that impacts response to SSRIs.

Promoter variants lead to altered transporter production

Response to SSRIs is influenced by number of LA versions of SLC6A4

2 copies of LA version – Normal responders
Expected response to SSRIs

1 copy of LA version – Intermediate responder
Possible increased risk of poor response and adverse events

0 copies of LA version – Poor responder
Increased risk of poor response and adverse events
What is MTHFR?

- The *MTHFR* gene codes for an enzyme called methylenetetrahydrofolate reductase. Methylenetetrahydrofolate reductase is converts the B-vitamin folate to 5-methyltetrahydrofolate, the form that can get into the brain.

  - Methyl-folate is involved in the synthesis of serotonin.

- As many as 20% of the population has inherited a defective copy of MTHFR and thus do not get adequate amounts of folate across the blood-brain barrier to support optimal function.

  - These patients have an increased risk of depression, and also may predispose them to be resistant to medical treatment.

  - In these patients, methyl-folate supplementation may enhance response to antidepressant therapy (e.g. Deplin).
Currently Available Pharmacogenetic Metabolic Markers

• Cytochrome P450 Hepatic Isozymes

  • Modify drugs so that they are polar and can be eliminated by the kidneys (e.g. hydroxylation)

  • CYP isozymes that are important in the metabolism and elimination of commonly prescribed drugs include: CYP2D6, CYP2C9, CYP2C19, CYP3A4, CYP3A5, CYP2B6, and CYP1A2
Dose relationship between blood concentrations of drug and efficacy and toxicity (single-dose)

- High response
- Toxic effects
- Therapeutic effects
- Sub-therapeutic effects
- Low response

Dose range (low → high)
**Metabolic Genes**

Variation in the metabolic genes CYP2D6, CYP2C19, and CYP1A2 can lead to higher or lower concentrations of drugs. Since recommended dosing assumes normal metabolism, individuals with genetic variants that impact drug metabolism may require dose adjustments or, in some cases, should avoid drugs impacted by genetic variants.
Normal metabolism of drug

Plasma Drug Concentration

Repeated doses over time

Minimum toxic concentration

Most or all of time spent with safe and effective levels

Minimum effective concentration
Poor metabolism of drug

- Plasma Drug Concentration
- Most or all of time spent with toxic dose levels
- Minimum toxic concentration
- Minimum effective concentration

Repeated doses over time
Ultra rapid metabolism of drug

- Plasma Drug Concentration
- Minimum toxic concentration
- Minimum effective concentration
- Most or all of time spent with levels below efficacious dose
How can pharmacogenetic testing be implemented into standard clinical practice?

• Commercial test providers offer panels of genetic tests that provide information regarding the potential response of individual patients to pharmacotherapy based upon their genetic makeup and the influence of genetics on drug response.

• The information provided by testing multiple gene variants provides much more useful guidance for therapeutic selection than any individual gene.

• This information can help prescribers select the right drug at the right dose for a given patient.
Most tests are conducted via buccal swab and provide quick and painless sample collection and processing.
What is the appropriate time to utilize pharmacogenetic testing?

Initial medication selection: For patients currently not on medication

Treatment switch: Poor efficacy, tolerability, or satisfaction

Severe treatment failure: Exacerbations of underlying conditions, serious adverse events, hospitalizations

GENETIC TESTING IS NOT RECOMMENDED FOR PATIENTS EXHIBITING AN ACCEPTABLE CLINICAL RESPONSE TO CURRENT THERAPY
Thank You!

Bill W. Massey, Ph.D.

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bill.massey@northwestern.edu
Your patients are unique
They deserve personalized treatment
Accountability, Efficacy and Outcomes

Prepared for:

Timothy Ramsey
VP, Product Development
SureGene, LLC
Open Minds, June 4th, 2014
SureGene Background
• 20 years of psychiatric genetics R&D

• Company turned 10 last month

• Focus on efficacy and outcomes
In a real world setting, testing improves outcomes across disease states and symptoms

- A review of routine practice in large Neuropsychiatry practice

- Diverse diagnoses
  - Diagnosis is not important, symptoms are!

- Tested patients experienced better outcomes / efficacy than untested patients
  - Only in symptom dimensions for which test results could impact drug selection
SSRIs – 90% of prescriptions were suboptimal

SNRIs – At least 42% of prescriptions were suboptimal

TCAs – 42% to 80% of prescriptions were suboptimal for common drugs

Antipsychotics – 51% were suboptimal

Olanzapine – 100% were suboptimal

Aripiprazole - 55% were suboptimal

Risperidone - 55% were suboptimal

Quetiapine – 29% were suboptimal
PGx testing is cost-effective

- PGx testing saves money
  - Herbild et al 2013 demonstrated that PGx testing saved on the order of $5,000 / yr for schizophrenia / schizoaffective
  - Olgiati et al 2012 showed that PGx test should be cost effective in developed economies for major depressive disorder

- SureGene’s analysis shows that SULT4A1-1 testing and guided therapy should save ~ $5,000 / yr in patients with a history of hospitalizations
Why is PGx testing cost-effective? An example

- Major metropolitan hospital system
- 30 day readmission rate 20-25%
- Rehospitalizations cost 5X to 10X as much as the initial event
- Payers may not pay for a reoccurrence within 30 days
- Cost of readmits exceeds total payments for initial visits
Outcomes matter – a case history

• Male in early 20s experiences severe psychotic break

• Forced hospitalization, non-responsive to medication with long term, court ordered commitment planned

• Tested with STA²R panel and was SULT4A1-1 positive

• Within days of beginning treatment with olanzapine was released to a transition facility

• New doctor switched antipsychotic leading to relapse and hospitalization within days

• Switched back to olanzapine and was quickly released
Personalized Medicine: Is Now the Horizon?

June 4, 2014

Where there is no path we make one.
Who is Genomind?

Genomind Overview

- Founded in 2009 to improve diagnostics and therapeutics in neuropsychiatry
  - Co-founders: Dr. Ronald Dozoretz and Dr. Jay Lombard
- Developed and commercialized the Genecept™ Assay, a patent-protected, saliva-based genetic test that informs clinician treatment decisions for patients with psychiatric conditions
- Expanding to Genecept Assay 2.0 by incorporating additional genes for brain wellness
- Licensed biomarkers from Emory University for early risk assessment of Alzheimer’s
- Investigating other biomarkers for neuropsychiatry
“Inspire patient-centric health by translating personalized medicine to neuropsychiatry.”
## Scientific Advisory Board, International Thought Leaders

<table>
<thead>
<tr>
<th>Name</th>
<th>Institution/University/Position</th>
<th>Expertise</th>
</tr>
</thead>
<tbody>
<tr>
<td>Roy H. Perlis, MD, MSc</td>
<td>Massachusetts General Hospital, Harvard Medical School</td>
<td>Heads international consortium to study genetics of antidepressant response, identified first genetic association with treatment resistance in major depression.</td>
</tr>
<tr>
<td>Scott T. Aaronson, MD</td>
<td>Sheppard Pratt, University of Maryland School of Medicine</td>
<td>Associate Medical Director at the Retreat at Sheppard Pratt, a premiere, self-funded psychiatric setting, and specialist for treatment resistant disorders.</td>
</tr>
<tr>
<td>P. Murali Doraiswamy, MD</td>
<td>Duke University Medical Center</td>
<td>Globally recognized researcher focused on intervention and treatment for Alzheimer’s and other memory disorders.</td>
</tr>
<tr>
<td>Maurizio Fava, MD</td>
<td>Massachusetts General Hospital, Harvard Medical School</td>
<td>Regarded as one of the foremost psychopharmacologists in the world and a leading expert on the role of medical foods in psychiatry.</td>
</tr>
<tr>
<td>Allan I. Levey, MD, PhD</td>
<td>Chairman of Department of Neurology, Emory University</td>
<td>Member of the prestigious National Alzheimer's Coordinating Center. The Institute for Scientific Information identified him as one of the most highly cited scientific researchers worldwide.</td>
</tr>
<tr>
<td>Anil Malhotra, MD</td>
<td>Zucker Hillside Hospital, Albert Einstein College of Medicine</td>
<td>Regarded as one of the world’s leading authorities on the genetics of schizophrenia and response to treatment. Primary area is genetics of the dopamine receptor.</td>
</tr>
<tr>
<td>Stephen M. Stahl, MD, PhD</td>
<td>University of CA, San Diego</td>
<td>Founder of the Neuroscience Education Institute, the leader in neuroscience education.</td>
</tr>
<tr>
<td>Rudolph E. Tanzi, PhD</td>
<td>Mass General Institute for Neurodegenerative Disease</td>
<td>Research investigating the genetic causes of Alzheimer's, including discovery of 3 genes causing early-onset familial AD.</td>
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Genomind has demonstrated the ability to develop and deliver pharmacogenomic science and services into mainstream neuropsychiatry:
25% of American experience major depression in their lifetime

189 million prescriptions written for depression, costing $12 billion in 2010

10% of 65-year-olds will be diagnosed with dementia

25% of 75-year-olds will be diagnosed with Alzheimer’s

Rates of ADHD increased 3% per year from 1997 to 2006 and 5% since then

In 2007, 10% of American children aged 4-17 are or have been diagnosed with ADHD

Growing rates of addiction
The Cost Burden of Mental Illness

Mental illness is the #1 risk factor driving employer health expense, surpassing obesity, high blood sugar, and high blood pressure.

TRD patients have annual healthcare costs that are 358% higher.

20% of patients with myocardial infarction have been diagnosed with major depression prior to the event.

68% of adults with mental health disorders have medical conditions.

Heartache and Heartbreak: Link between depression and cardiovascular disease.
Treating Psychiatric Disorders

Clinical Challenges:

- Diagnosis is often purely symptomatic
- Frequent comorbidity increases incidence of side effects, drug-drug interactions and poor therapeutic response
- Failure of multiple treatment trials, despite wide array of psychotropic treatment options

The result:
A trial and error approach to treatment
Biomarkers: A Growing Tool Box

Gene Based:
- Single Nucleotide Polymorphisms (SNPs)

Epigenetics:
- Methylation
- Acetylation

Gene Expression and Proteins

Brain Imaging
### When Can Biomarkers Help in Clinical Settings?

Genetic testing may aid in the treatment of patients with:

- Treatment resistance
- Previous failed treatment trials with adverse events or poor response
- Polypharmacy
- Comorbidity
- Complex or uncertain diagnosis
- Noncompliance or issues with medication adherence
Available Now – The Genecept Assay
The Genecept Assay

Genecept Assay introduced commercially in 2010:

- Patented gene-based assay informs treatment decisions for patients with mental health conditions, such as depression, anxiety, bipolar disorder, schizophrenia, ADHD, and chronic pain
- Neurotransmitter based genes, including serotonin, dopamine, and glutamate
- Pharmacokinetic genes related to drug and nutritional metabolism

Over 18,000 patients have used the test in the US

Over 1,200 clinicians have ordered the test for patients

More than 2 of every 3 clinicians who order one test subsequently order for another patient

Clinicians are using the Assay as a standard of care in their practices

- Clinicians initially used Genecept for more treatment resistant patients; however, the number of patients tested with no previous treatment trials has doubled since launch
The Process – Genecept Assay

1. Patients provide 1ml of saliva into a plastic specimen kit manufactured by our partner DNA Genotek

2. An overnight shipping packet & barcoded requisition are provided so the patient sample can be sent securely to our lab

3. Our CLIA and CAP certified lab performs our proprietary panel of genetic tests focusing on neurotransmitter and metabolism pathways

4. A patented algorithm results in an online analytical report delivered to a clinician within 3-5 days to inform treatment decisions

5. Genomind certified physicians, Ph.D.’s and Pharm.D.’s are available to discuss results with treating clinicians via telephonic consult

Results of the test, combined with expert clinical consultations, help to achieve better patient responses to treatment
Genecept Assay Report

**Summary**

Genecept® is a commercial brain health test that is used to measure brain health and cognitive function. The test involves a battery of cognitive tasks that assess various aspects of brain function, including memory, attention, language, and executive function.

**Results**

The test results are presented in a detailed report, which includes a comparison of the test results to normative data and a summary of the patient's cognitive performance. The report also provides recommendations for improving brain health and cognitive function.

**Appendix**

The appendix contains additional information, such as a glossary of terms and a list of references for further reading.

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### Executive Summary

The Genecept® test was administered to the patient on October 1, 2012. The patient's performance was compared to normative data, and the results were discussed in detail. The patient was advised to engage in brain-healthy activities to improve cognitive function and maintain brain health.

### RESULTS REPORT

| Patient | A. Patient | Gender | Age | Ethnicity | Education | Occupation | Years of Education | Years of Work Experience | Test Date | Test Administration
|---------|------------|--------|-----|-----------|-----------|------------|-------------------|--------------------------|-----------|----------------------|
|         |            | Male   | 50  | White     | Bachelor  | Professional|                  |                          | October 1, 2012 | Face-to-face

### Glossary

- **Cognitive Function**: A broad term that encompasses various mental processes, including memory, attention, language, and executive function.
- **Memory**: The ability to encode, store, and retrieve information over different periods of time.
- **Attention**: The ability to focus on a task or stimulus while excluding distractions.
- **Language**: The ability to understand and use language to communicate effectively.
- **Executive Function**: A group of cognitive skills that allow individuals to plan, organize, and monitor their behavior to achieve goals.

### References


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**Note**

The Genecept® test is a valuable tool for assessing brain health and cognitive function. However, the test results should be interpreted in the context of the patient's medical history, lifestyle, and other factors that may influence cognitive performance. Consultation with a healthcare provider is recommended to determine the best course of action based on the test results.
Welcome to the Genomind Clinician Portal. Designed with you in mind, this portal provides secure online access to patient reports and clinical tools. Here you can access and review your patients’ Geneccept Assay test results, or learn more about Genomind and the research studies underway.

The portal is also the home of our Open Label Study of Clinical Utility and Patient Outcomes of the Geneccept Assay, our recently launched study created to help improve personalized therapies for difficult-to-treat patients. Participating clinicians can complete the three (3) surveys here.

If you are interested in learning more about the study or participating, please let us know. Issues, questions, or bugs? Please call us at 877-395-8858 or email CustomerService@genomind.com for portal assistance.

Studies

The Geneccept Assay is currently the focus of several clinical research trials. As a clinician, your participation could help us better understand how personalized medicine affects treatment decisions and may improve outcomes for patients with psychiatric illnesses. Click HERE to find out more!
Genomind’s Clinical Consultation: Integrated Treatment Planning

- Personalized access to consultations with Genomind certified physicians, Ph.Ds and Pharm.Ds for every results Report – no additional charge

- Creates significant connection among the patient, their clinical history, their genetic results, and the treating clinician

- Enhances continuing education of biomarkers and translation of genetic results to potential treatment strategies

- Can also be used for the clinician’s family consultations and program discharge planning
Genecept™ Improves the Traditional Clinical Pathway to Treat Depression

**Traditional Treatment**

- **Preliminary Diagnosis**
  - Treat with SSRI or SNRI
  - (+) dose of SSRI/SNRI if no ADR
  - Substitute different SSRI or SNRI
  - Consider augmentation
  - Consider different therapies
  - ECT or VNS

  - Assess side effects at **week 2**
  - Assess response at **week 4**
  - Assess side effects at **weeks 6-8**
  - Assess response at **weeks 8-10**
  - Assess side effects at **week 16**
  - Assess response at **weeks 18-24**
  - If indicated, ECT or VNS would occur at appx 5-6 months

  - Book appt (assuming availability) week 12-14

**TOTAL DIAGNOSIS/TREATMENT TIMELINE: 5-6 MONTHS**

**Treatment with Genecept™ Assay**

- **Preliminary Diagnosis**
  - Use Genecept™ Assay to determine proper treatment

**Genecept™ Assay to determine proper treatment**
# Genes in the Genecept Assay

<table>
<thead>
<tr>
<th>GENES</th>
<th>ROLE</th>
<th>CLINICAL CONNECTION</th>
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<tbody>
<tr>
<td>Serotonin Transporter (SLC6A4)</td>
<td>Responsible for reuptake of 5HT from the synapse</td>
<td>Inhibition of this protein by SSRIs, SNRIs, and TCAs</td>
</tr>
<tr>
<td>Serotonin Receptor (SHT2C)</td>
<td>G-protein coupled receptor activated by serotonin to release dopamine and norepinephrine</td>
<td>Associated with satiety signaling and impact on antipsychotic weight gain</td>
</tr>
<tr>
<td>Dopamine Receptor (DRD2)</td>
<td>G-protein coupled receptor activated by dopamine in the brain</td>
<td>Target binding site for antipsychotic medications</td>
</tr>
<tr>
<td>Gated Calcium Channel (CACNA1C)</td>
<td>Regulates entry of calcium into cell</td>
<td>Mood stabilizers target excitatory neurotransmission</td>
</tr>
<tr>
<td>Ankyrin G (ANK3)</td>
<td>Necessary for action potential firing of gated sodium channels</td>
<td>Mood stabilizers target excitatory neurotransmission</td>
</tr>
<tr>
<td>Catechol-O-Methyltransferase (COMT)</td>
<td>Responsible for degradation of dopamine and norepinephrine</td>
<td>Reduced or increased dopamine states can have emotional and behavioral effects</td>
</tr>
<tr>
<td>Methylenetetrahydrofolate reductase (MTHFR)</td>
<td>Predominant enzyme which converts folic acid to active form of folate (methylfolate)</td>
<td>Methylfolate is a precursor for synthesis of catecholamines and is important for DNA methylation</td>
</tr>
<tr>
<td>Metabolism (CYP2D6, CYP2C19, CYP3A4)</td>
<td>Enzymes that metabolize medications in the liver</td>
<td>Large number of psychiatric medications are substrates of the 2D6, 2C19 and 3A4 systems</td>
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PK and PD Genes

Pharmacokinetic Genes: impact on drug concentration
Pharmacodynamic Genes: impact on target site
Clinical Studies and Data
Patient Diagnoses (N = 661)

- 48% Depression
- 15% Anxiety
- 10% Bipolar
- 25% ADD/ADHD
- 1% Schizophrenia or schizoaffective disorder
- 1% Cognitive disorders including dementia, or delirium
73% of patients failed 2 or more adequate medication trials prior to Genecept.
Patients reporting not having a euthymic period for over a year: 60.0%

Reported patients had two or more previous treatment trials: 75.0%

Indicated the report influenced their treatment: 87.0%

Indicated the report increased their confidence in treatment decisions: 93.0%

Elected to make changes to patient treatment: 76.0%
**Resource Utilization Study**

**Design:** Retrospective claims review of patients who utilized the Genecept Assay compared to propensity-scored matched controls

- Partnership with IMS Health - foremost provider of healthcare information
- \( N = 333 \) (resource utilization) and 454 (med adherence)

**Findings:**

- **9.5%** relative cost savings and
- **6%** greater medication adherence

in Genecept patients as compared to matched controls

Fagerness et al. in press in the *American Journal of Managed Care*, May 2014
Change in Healthcare Utilization and Medication Adherence Over 4 Months Post Genecept

Results - Resource Utilization & Adherence

- Pharmacy Activity: 14.2% (Genecept Patients) vs. 5.5% (Controls)
- Private Practitioner Activity: 63.4% (Genecept Patients) vs. 0.3% (Controls)
- Medication Adherence: 6.3% (Genecept Patients) vs. -26.8% (Controls)
Clinicians Report Improved Outcomes

90% of treatment resistant patients show clinically measurable improvement

All Patients (N=661)  ≥2 Previous Adequate Treatment Trials (N=482)
Patients Report Improved Outcomes

Patient reported Depression, Anxiety and Medication side effects showed significant decreases, and Quality of Life a significant increase (N=146)

**QIDS: Depression**
- Baseline: 14
- One Month: 12
- Three Months: 10

**QLESQ: Quality of Life**
- Baseline: 38
- One Month: 46
- Three Months: 54

**UKU: Side Effects**
- Baseline: 28
- One Month: 20
- Three Months: 12

**Zung: Anxiety**
- Baseline: 31
- One Month: 27
- Three Months: 20

P < 0.01
On the Horizon - The Genlighten™ Assay for Early Risk Assessment for Alzheimer’s
Incidence of Alzheimer's and Pre-Dementia

- Over 5 million Americans are living with Alzheimer’s disease – 1 in 8 who are 65 and older
- Someone in the US will develop Alzheimer’s every 68 seconds
- It is the 6th leading cause of death – and 1st for diseases with no known cure
- Average medical costs for MCI is $6,500/yr compared to $3,000 year for non-MCI patients
- Payments for care estimated to be $200 billion in the US alone – rising to $1 trillion by 2050
- Worldwide, 26.6 million people had AD in 2006 – increase to 65mm by 2030

Genlighten™ Assay: Novel Protein Biomarker Test

- Blood-based protein biomarker test for early risk identification of Alzheimer’s Disease
- Biomarker validated for specificity and sensitivity
- Licensing agreement with Emory University for Genomind to commercialize the test
- Can provide intervention alternatives, including non-pharmacological
- Commercialization planning underway, with immediate steps:
  - Data validation
  - Lab partner discussions
  - Code, coverage, and reimbursement investigation
Genlighten Disrupts the Traditional Clinical Pathway to Treat Dementia

Traditional Treatment

Patient has memory/mood complaint → Referral to neurologist → Orders MRI/NP testing → May order PET scan or spinal tap → Prescribes CI or memantine → Disease progresses unremittingly

Treatment with Genlighten

Patient has memory/mood complaint → Test blood with Genlighten → If positive, use stepped up diagnostic protocol and potential interventions → Disease modifying therapy slows or inhibits disease progression
Personalized Medicine – The Promise

- Improve Efficacy with Targeted Rx Selection and dosing
- More information to understand complex diagnoses
- Avoid drug-drug interactions
- Reduce Side effects
- Increase Compliance

- Treatment Resistance
- Comorbidity
- Complex Diagnoses
- Polypharmacy
- Side Effects & Nonadherence
Personalized Medicine – The Challenge

Clinical validation

- Continuous data collection and study of patient outcomes – when “enough” data?
- Gold standard of Randomized Controlled Trials (RCTs) yet value of “N’s of 1”, especially in psychiatry

Reimbursement

- A Black Box – no standard data requirements for coverage and reimbursement decisions
- MDx as a cost or cost savings?
- “Payer Fatigue” over the Next New (Wonderful) Innovative Treatment(s)(s)

Regulatory

- CLIA now, FDA someday?
- How to “inform” consumers without “selling” to them?
- The protective “3 M’s” (Medicare, Medicaid, Military), yet populations of great need
Would Freud Have Used Biomarkers?
On to the Horizon!
Where there is no path we make one.
Personalized Medicine at The Menninger Clinic

OPEN MINDS Institute
Ben Weinstein, MD
Assessment Division Director
June 4, 2014
What is The Menninger Clinic

• National Depression Center
• Quaternary Referral Center for mental health care.
• Private Not for Profit. Outside the insurance industry structure.
• Tradition of excellence in milieu and psychodynamic psychotherapy
• Embraces evidence based treatments such as DBT, ACT, CBT, CAMS
Advancing treatment. Transforming lives.

Who do we treat?

- Treat complex and “treatment resistant” patients
- More intense treatment leads to improved outcomes
- 2% of US population in 12 month period experience severe depression
- Suicide was the 10th leading cause of death in 2010
- Mental Illness direct cost $150B, lost wages $193B, $150B other services
Comprehensive Psychiatric Assessment and Stabilization

- Complex medical, neurological, and psychiatric illnesses
- Many episodes of prior treatment with limited or no success
- Often enter treatment feeling “I’ve tried everything and it doesn’t work for me.” Many patients had completed greater than 3 adequate treatment trials.
Comprehensive Psychiatric Assessment and Stabilization

- Clarify diagnosis
- Guide appropriate treatment
- Why aren’t these patients responding to treatment?
Pharmacogenetics

• Can genes help explain poor response or adverse effects?
• Pharmacodynamic – what medications do to us
• Pharmacokinetic – what we do to medications
Case Example 1

Woman in her 30’s with depression and anxiety. Poor response and high frequency of side effects. Unable to tolerate SSRIs.
Case Example 1

Woman in her 30’s with depression and anxiety. Poor response and high frequency of side effects. Unable to tolerate SSRIs.

- SLC6A4 (Serotonin transported gene) the site of action of all SSRIs
  - “Long Gene” favorable response
  - “Short Gene” poor response and more side effects
  - This patient was Short/Short
Case Example 1

Woman in her 30’s with depression and anxiety. Poor response and high frequency of side effects. Unable to tolerate SSRIs.

- **SLC6A4** (Serotonin transported gene) the site of action of all SSRIs
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- **CYP2D6 Gene** (liver enzyme system that metabolizes most SSRIs)
  - Ultrarapid, Extensive, Intermediate, and Poor
  - This patient actually lacked the genes = no metabolizer.
Case Example 1

Woman in her 30’s with depression and anxiety. Poor response and high frequency of side effects. Unable to tolerate SSRIs.

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- CYP2D6 Gene (liver enzyme system that metabolizes most SSRIs)
  - Ultra rapid, Extensive, Intermediate, and Poor
  - This patient actually lacked the genes = no metabolizer.

- Changed medication approach (Monoamine oxidase inhibitor)
  - Improved tolerability and efficacy
  - Reduced feeling of hopelessness
Case Example 2

Gentleman in 20’s with anxiety and ADHD. Became acutely psychotic when treated with stimulants.
Case Example 2

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• Changed medication approach (non-stimulant)
  • Improved efficacy
  • No psychosis
Effect on treatment

- “Medical-izes” their condition
- Helps patients to have a possible reason for lack of response
- See themselves as less “broken”
- Inspires hope – but must temper expectations
Why wait?

- Could this be helpful for the other programs?
- When some of the patients were tested, ALL wanted to be tested.
- Why limit this to people that have not responded?
- Why not give everyone their best chance to respond, the first time.
- Now offer Genomind to all patients admitting to Menninger
- Overwhelming number of patients agree to and value test
Thank you.
Questions & Discussion
Discussion Questions

- What does your current customer base look like – who is using personalized medicine products?
- Where do you see personalized medicine fitting into the future standard of care?
- What are the reimbursement issues Value proposition and clinical utility of these tests?
- Are there any payers currently covering genomic testing? Where do you see the future of reimbursement when it comes to personalized medicine?
The market intelligence to navigate. The management expertise to succeed.