Precision Medicine at Intermountain Healthcare

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Intermountain Healthcare
Precision Medicine at Intermountain Healthcare: An Overview

- Clinically implementing precision oncology
- The survival and cost outcomes associated with precision oncology
- Precision Medicine in other medical disciplines outside of oncology
Intermountain Healthcare: An Integrated System

- **22** Hospitals
- **2,800** Licensed Beds
- **180** Medical Group Clinics
- **875,000** SelectHealth Members
Precision Oncology Workflow

Day 1: Clinic
Day 2-4: Biopsy or FFPE
Day 5: Pathology Review
Day 6: Sample Prep
Day 7: Molecular Analysis (NGS)
Day 8: Bioinformatics
Day 9: Molecular Tumor Board
Day 10: Results and Treatment
MTB Interpretation included on the report

Interp. in the report

Based on the genomic profile of your patient's tumor, the Molecular Tumor Board's interpretation suggests the following potential therapeutic interventions in the ranked list below:

- **EGFR**
  - Afininib
  - Erlotinib

*Order*
Patient Case: HER2+ Colon Cancer

- 47 yo man with metastatic colon cancer
- Genomic analysis: HER2 amplification

Nadauld et al, JCO-PO, 2017
Patient Case: HER2+ Colon Cancer

- Time to response: 2 months
- Total time on drug: 18 months

Nadauld. JCO-PO. 2017
Intermountain Precision Medicine Cohort Study

Patients received standard trx within Intermountain

36 standard trx
match: dx, age, gen, #prev. trx

Assess:
-PFS
-Cost of care

61 with actionable mutation, and received targeted trx

36 genomics+trg trx
match: dx, age, gen, #prev. trx

Assess:
-PFS
-Cost of care

25 without match: dx, age, gen, prev. trx

Haslem and Nadauld. JOP. 2016
Precision Oncology: Overall Survival

- Standard chemotherapy (n=22): Avg. = 11.0 wks PFS, Avg. = 25.8 wks overall survival
- Targeted cancer therapy (n=22): Avg. = 21.4 wks PFS, Avg. = 51.7 wks overall survival

Haslem et al., Oncotarget. 2018
### Precision Oncology Costs

<table>
<thead>
<tr>
<th></th>
<th>Control (N=22)</th>
<th>Targeted (N=22)</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inpatient</td>
<td>$552</td>
<td>$448</td>
<td>($104)</td>
</tr>
<tr>
<td>Outpatient</td>
<td>$2,376</td>
<td>$1,167</td>
<td>($1,209)</td>
</tr>
<tr>
<td>ER</td>
<td>$34</td>
<td>$45</td>
<td>$11</td>
</tr>
<tr>
<td>Rx drugs</td>
<td>$346</td>
<td>$940</td>
<td>$594</td>
</tr>
<tr>
<td>Hospice</td>
<td>$146</td>
<td>$9</td>
<td>($137)</td>
</tr>
<tr>
<td>Sequencing</td>
<td>$0</td>
<td>$112</td>
<td>$112</td>
</tr>
<tr>
<td><strong>Total/week</strong></td>
<td><strong>$3,453</strong></td>
<td><strong>$2,720</strong></td>
<td><strong>($734)</strong></td>
</tr>
</tbody>
</table>

Haslem et al., Oncotarget. 2018
### Precision Oncology Costs

#### Costs per patient among Select Health members in the last 3 months of life, by site of care

<table>
<thead>
<tr>
<th></th>
<th>Total</th>
<th>Inpatient</th>
<th>Outpatient</th>
<th>Office</th>
<th>Rx Pharmacy</th>
<th>ER/UC</th>
<th>All other</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SelectHealth - Standard Tx</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>$46,940</td>
<td>$29,523</td>
<td>$7,425</td>
<td>$3,663</td>
<td>$1,415</td>
<td>$1,385</td>
<td>$1,177</td>
</tr>
<tr>
<td><strong>SelectHealth - Targeted Tx</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>$43,711</td>
<td>$15,535</td>
<td>$11,216</td>
<td>$6,265</td>
<td>$5,500</td>
<td>$1,469</td>
<td>$1,242</td>
</tr>
</tbody>
</table>

-6.9%  -47.4%  51.1%  71.1%  288.7%  6.1%  5.5%
(n=1,721)  (n=93)
Genomic Testing now covered by local health plan

GENETIC TESTING: MOLECULAR PROFILING FOR DETERMINING THERAPY OF MALIGNANT TUMORS

Commercial Plan Policy

SelectHealth covers multi-marker tumor panels using next generation sequencing in the diagnosis and treatment of cancer as a method to guide the selection of therapeutic agents for malignant tumors in limited circumstances.

Patients must meet ALL of the following to be eligible for next-generation sequencing:

1. The member has one of the following clinic circumstances.
   a. Any advanced stage IV solid tumors;
   b. All lymphomas;
   c. Multiple myeloma.
2. Patient has demonstrated progression of disease despite at least 1 lines of FDA approved and NCCN approved standard cancer therapy.
3. Member has performance level as evidence by documentation of ECOG performance status 0-2 or Karnofsky score ≥70°
4. Advance care planning (ACP) has been completed, and documented, with a trained facilitator (i.e. nurse navigator, licensed clinical social worker) or a palliative care provider, or the treating provider.
Precision Medicine Menu

**ICG100™**
Cancer Panel

**RxMatch™**
Pharmacogenomics in Mental Health

**HerediGene™**
Hereditary Cancer Panel

All orderable and reportable within the EMR (Cerner)
ICG100™ Precision Cancer Test:  *Product + Impact*

**Overall Survival:**
- **Precision Med**: 51.7 weeks
- **Control**: 25.8 weeks
- **HR**: 0.53, \( p < 0.002 \)

**Cost of Care:**
- **Precision Med**: $3,453/week
- **Control**: $2,720/week
- \( p = 0.22 \)

*Figure 1. Overall survival, \( p = 0.002 \)*
Consider ordering RX Match for depression and anxiety in:

1. New diagnosis of depression and/or anxiety to be treated with an antidepressant

2. Existing diagnosis of depression and/or anxiety not responding
HerediGene™: Hereditary Cancer Test Product + Impact

10% of all cancers are due to a gene mutation that can be passed through a family.
System Wide Genetic Counseling: *Product + Impact*

Reduced time to genetic counseling appointment

12 days → 6 days
Translational Science Center
High Throughput Genomics Facility

Illumina NovaSeq 6000
- 15,000 whole genomes at 30X per year

WGS, WES and Transcriptome

Chromium 10X Genomics Instrument
- Haplotyping and single cell sequencing

Fluidigm Helios/Hyperion Mass Cytometer

Lab Automation – Hamilton Stars

Full LIMS integration (LabVantage)

CLIA/CAP certification 2H 2018
NGSOne: Whole Genome Product + Impact

- Whole Genome, Whole Exome Sequencing, Whole Transcriptome
- New external collaborations
- NICU sequencing
- Precision Nephrology
- Biorepository (4.3M archival samples)
Precision Genomics across all Clinical Programs and Services
Acknowledgements

- Intermountain Precision Genomics:
  - Derrick Haslem
  - Gary Stone
  - Pravin Mishra
  - David Loughmiller
  - Genomics Core Lab
  - Cancer Clinical Program
  - Sharanya Raghunath
  - Jason Gillman
  - Robin Romero
  - Brent James

- Stanford University
  - Jim Ford
  - Hanlee Ji

- NCI
- AACR
- ASCO
Pharmacogenetics and Hospital Readmissions

Number of Home Health Patients Assessed for Eligibility (N=655)
Obtained informed consent; screened potential subjects by inclusion & exclusion criteria; obtained history, document. Inclusion criteria: Aged 50 & older, admitted to Home Health after hospitalization, taking or starting one of 55 medications associated with genetic risk in YouScript®; Exclusion criteria: Previous CYP testing, history of organ transplant, current malabsorption, treatment of invasive solid tumors or hematologic malignancies in the last year, ESRD, dialysis.

Number Excluded (N=545)
- Not meeting inclusion criteria (N=412)
- Refused to participate, refused Home Health, clinician would not order pharmacogenetic testing, already enrolled, other reasons (N=133)

Number Randomized (N=110)

Arm 1
No Genetic Testing Performed. Made Medication Therapy Recommendations Based on Known CYP P450 DDI using standard Drug Information Sources
Assigned to Not Receive Intervention (N=53)

Arm 2
Genetic Testing Performed. Made Medication Therapy Recommendations Based on YouScript® Clinical Decision Support Tool for DDI, DGI & DDGI
Assigned to Receive Intervention (N=57)

Elliott, L., *PLOS One*. 2017
Decreased re-hospitalization and ED visit rates

Elliott, L., *PLOS One*. 2017
Pharmacogenetics: Opioids as an example

<table>
<thead>
<tr>
<th>Therapeutic Class</th>
<th>Standard Precautions</th>
<th>Caution / Info</th>
<th>Change recommended</th>
</tr>
</thead>
<tbody>
<tr>
<td>Opioids</td>
<td>Buprenorphine, Fentanyl, Hydrocodone</td>
<td>Codeine, Fentanyl (OPRM1), Oxycodone, Oxycodone (CYP3A5)</td>
<td>Tramadol</td>
</tr>
<tr>
<td>Hydrocodone</td>
<td>CYP2D6: *4/*35</td>
<td>Typical response is expected; no additional therapeutic recommendations.</td>
<td></td>
</tr>
<tr>
<td>Oxycodone (Oxycontin)</td>
<td>CYP2D6: Intermediate metabolizer. One allele showing normal activity and one showing little or no activity.</td>
<td>Individuals with intermediate metabolizer status are at risk of potentially reduced efficacy; consider alternative therapy. Insufficient evidence to allow calculation of dose adjustment. Select alternative drug (not tramadol or codeine) or be alert to symptoms of insufficient pain relief.</td>
<td>Efficacy</td>
</tr>
</tbody>
</table>
RxMatch™

- Identifies how a patient metabolizes medication.
- The RxMatch report guides medication selection and dosing for prescribing providers.