The Clinical Implementation of Precision Cancer Medicine

HIMSS 2017
Precision Medicine IT Solutions – Driving Clinical Quality and Value

Mark Lewis MD
Director, Gastrointestinal Medical Oncology
Intermountain Healthcare
Overview

- Challenges in Precision Cancer Medicine
- Intermountain Clinical Cancer Genomics Program
- IT Platform and Architecture
Identify and Target Genomic Alterations

Variants
1. FGFR1
2. P53
3. MEK1
4. EGFR
5. HER2

*drug 1*
*drug 2*
*drug 3*
*drug 4*

Cancer cell
Genomic analysis
Is it really that simple?
Tumor Heterogeneity
Tumor Evolution

Mutations driving relapse present at low frequency

Anticipation-based chemotherapy

Puente, Nat. Genet., 2013
Number of Mutations in Human Cancers

A. 
- Glioblastoma (14)
- Medulloblastoma (8)
- Rhabdoid cancer (4)
- Neuroblastoma (12)
- Acute lymphocytic leukemia (11)

B. 
- Non-Hodgkin lymphoma (74)
- Breast cancer (33)
- Hepatocellular cancer (38)
- Pancreatic cancer (45)
- Lung cancer (non-small cell) (147)
- Lung cancer (small cell) (163)
- Esophageal adenocarcinoma (57)
- Esophageal squamous cell carcinoma (79)
- Gastric cancer (53)
- Colorectal cancer (66)
- Ovarian cancer (42)
- Endometrial cancer (49)
- Prostate cancer (41)
- Melanoma (135)
So Many Targets ...

B. Vogelstein, Science. 2013
Precision Cancer Medicine

1. Molecular Profiling

2. Prognostic Markers
   - Markers predictive of drug sensitivity/resistance
   - Markers predictive of adverse events
Intermountain Healthcare

- *Integrated, multidisciplinary healthcare system*
- *22 hospitals and 182 clinics*
- *"Open system" (facilities open to MDs & patients)*
- *Leader in value-based care (SelectHealth)*
Intermountain Cancer Genomics

- Personalized Medicine Clinic
- Genomic Testing
- Molecular Tumor Board
- Drug Procurement
- Outcomes and Cost Tracking

www.precisioncancer.org

HQ and core lab in St. George, UT
Molecular Tumor Board

- Multi-institutional participants
- Experts in Cancer Genomics
- Interpretation of Genomics
Building the Program: IT

- Robust internal data warehousing

- Multi-year EMR transition from homebrew to Cerner

- EMRs and data warehouses could not accommodate genomic data, precision medicine workflows, genomics CDS, & outcomes tracking

- Partnered with Syapse on Precision Medicine software platform
<table>
<thead>
<tr>
<th>PM Clinic</th>
<th>Day 1</th>
<th>Molecular analysis (NGS)</th>
<th>Day 7-8</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biopsy or FFPE</td>
<td>Day 2-4</td>
<td>Analytics</td>
<td>Day 9-11</td>
</tr>
<tr>
<td>Pathology Review</td>
<td>Day 5</td>
<td>Molecular Tumor Board</td>
<td>Day 12-13</td>
</tr>
<tr>
<td>Sample Prep</td>
<td>Day 6</td>
<td>Results and Treatment</td>
<td>Day 14-15</td>
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Clinical Cancer Genomics Workflow

- **Eligibility:** All Stage 4 Cancer Patients
- **Cancer Genomic Testing**
- **Molecular Tumor Board:** Treatment Guidance
- **Drug Procurement**
- **Outcomes Tracking**
- **Best Practice Updates**

**Decision Support:** Variant Interpretation

**Clinical Trial Enrollment**
Clinical + Genomics Data Integration

In-House Precision Genomics Lab

Sequencing & Report

Integrated repository of structured data

syapse

Clinical Systems

PACS
EMR
Data Warehouse
Drug Administration
LIS
CPOE
Registry
Clinical Data Integration

• *Source clinical data from:*
  • Intermountain data warehouse
  • Direct systems feeds (lab, imaging, pharmacy, analytics)

• *HL7 v3, FHIR, and Syapse API all leveraged for interoperability*

• *Ongoing: Cerner integration*
Interoperability Challenges

- **Defining standards for exchanging genomic data**
  - There is no industry standard for exchanging genomic data
  - Current integration with send-out labs via Syapse Lab Certification program to address clinical need for interoperability
  - HL7 Clinical Genomics group making great progress with FHIR - not used by labs yet

- **Need to be able to seamlessly use specialized tools like Syapse in EHR-based clinical workflow**
  - Built on SMART, CDS-hooks, etc.

- **No widely adopted way to exchange a patient’s cancer treatment history**
Genomics Data Standards

• Chose to build tumor genomics lab in-house to better control the data quality and standards. Outsource germline genetics labs, but assure data interoperability.

• Robust structured data capture of genomics assay results, interpretation, reports, and treatment guidance.

• Collaboratively developed genomics ontology with Syapse that has become standard for many other health systems.
Integrated Clinical and Molecular Data

**Clinical History**

- **Encounter Summary**
  - ECOG Score: 1 2 2 2 3 2 2 2 3 2 3 2 2 2 2 2 2
  - Encounters:
    - APR:  
    - MAY:  
    - JUN:  
    - JUL:  
    - AUG:  
    - SEP:  
    - OCT:  
    - NOV:  
    - DEC:  

- **Tumor Size**
  - Size(CM): [Graph showing tumor size over time]

- **Treatments**
  - Gemcitabine: [Graph showing treatment over time]
  - Carboplatin: [Graph showing treatment over time]
  - Trametinib: [Graph showing treatment over time]
# Genomic Data

## Detailed Report: TumorOme Dx (TRF-34)

### Patient Information

<table>
<thead>
<tr>
<th>Name</th>
<th>Jacob D. Moyer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient DOB</td>
<td>1954-04-11</td>
</tr>
<tr>
<td>Gender</td>
<td>Male</td>
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<tr>
<td>Patient ID</td>
<td>PT-15</td>
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</table>

### Specimen Information

<table>
<thead>
<tr>
<th>Surgical Procedure Date</th>
<th>04/02/2014</th>
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<tbody>
<tr>
<td>Specimen Source</td>
<td>Lung</td>
</tr>
</tbody>
</table>

### Physician Information

<table>
<thead>
<tr>
<th>Ordering Physician</th>
<th>Lincoln Naclaudi, MD, PhD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pathologist</td>
<td>Jeremy Wallentine, MD</td>
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</table>

## Molecular Tumor Board Interpretation

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:

<table>
<thead>
<tr>
<th>Tumor Board Recommendations</th>
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<tbody>
<tr>
<td><strong>Rank</strong></td>
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<tr>
<td>--------</td>
</tr>
<tr>
<td>1</td>
</tr>
<tr>
<td>2</td>
</tr>
<tr>
<td>3</td>
</tr>
<tr>
<td>4</td>
</tr>
</tbody>
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*This ranking is based on the interpretation of an expert panel and is not associated with specific clinical trial data.*

## Findings Associated with Approved Therapies

5 somatic mutations reported.
0 associated therapies approved for patient's tumor type.
2 associated therapies approved for other tumor types.
Molecular Tumor Board

Click to edit the recommendation
Clinical Decision Support

• Molecular Tumor Board reviews all cases, then enters guidance into Syapse software

• All interpretations are stored in a structured, semantic knowledge-base

• Interpretations can be re-used for clinically -- and genomically-- similar cases, enabling scale

• CDS provides community oncologists with treatment planning guidance
Clinical Decision Support
Specialty Pharmacy Integration

• Puts the “action” in precision medicine

• Enables automated drug procurement

• Specialty drug prescription and patient clinical + genomic data sent to Intermountain’s internal specialty pharmacy for processing

• Specialty drug procurement success rate is 80%
Specialty Pharmacy Integration

Guidance

Recommended Treatments

- **Tremelimum (Mekinist)**
  - RELEVANT VARIANTS: BRAF V600
  - Order

- **Everolimus (Afinitor)**
  - RELEVANT VARIANTS: STK11 Loss
  - Order

- **Temozolomide (Temodal)**
  - RELEVANT VARIANTS: STK11 Loss
  - Order

- **Dabrafenib (Depuy)**
  - RELEVANT VARIANTS: STK11 Loss
  - Order

Recommendation Notes

Patient should complete current course of first line chemotherapy and then be reassessed in 4 weeks.

Clinical Trials

- **A Study of Zealosar (Vemurafenib) in Patients With BRAF V600 Mutation-Positive Cancers**
  - NCT0154007
  - Order
  - Email

Prescription Order Form

INTERMOUNTAIN CANCER GENOMICS
PRESCRIPTION ORDER FORM
REQUESTED ON 04/17/2015
PATIENT: TEST-F5142807 TESTER DATE OF BIRTH: 1950-02-17

- **FIRST NAME**: Test-F5142807
- **LAST NAME**: Tester
- **MIDDLE INITIAL**: Date of Birth: 1950-02-17
- **PATIENT ID**: Pat-12345
- **STREET ADDRESS**: 101 Syaspe St
- **CITY**: Palo Alto
- **STATE**: CA
- **POSTAL CODE**: 93333
- **TRADE NAME**: Hecaprin
- **DOSE**: 2
- **NOTES**
Learn From Real-World Evidence

- Robust outcomes & cost tracking
- Ability to query all data at point of care
- Used in MTB to improve care recommendations
Precision Medicine Software: Point of Care

- Review patient’s molecular & clinical history
- Order and review molecular testing
- Receive clinical decision support & procure specialty drugs
- Coordinate care through an optimized workflow
- Learn and revise care plans over time
Program Outcomes

• 25x increase in patients receiving precision medicine: ~15% of total cancer population

• Specialty drug procurement success rates increased 5x, to 82%

• 64% of all patients had their care management changed

• Substantial clinical improvement and cost savings
Patient Case: Lung Cancer

- 56-year-old man with metastatic lung cancer

- Progressed through standard chemotherapy regimen

- Genomic analysis: BRAF mutation (not V600E)
Patient Case: Lung Cancer (cont’d)

- **Targeted treatment x 9 months**

Before

After
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
Study Outcomes

• *Progression-Free Survival*
  • Precision Medicine cohort = 22.9 weeks
  • Standard of Care cohort = 12.0 weeks

• *Total Cost of Care*
  • Precision Medicine cohort = $3,204 per week
  • Standard of Care cohort = $3,501 per week
Intermountain BioRepository

- 4 million archival samples
- Accumulated from 1975-present
- Longitudinal annotated healthcare outcome data (30+ years)
High Throughput Sequencing

- **Accommodated by HiSeq X10**
- **20,000 genomes per year**
- **Enables sequencing of our biorepository**
Oncology Precision Network (OPeN)

- Multi-institutional cancer genomics data consortium
- Inform point-of-care treatment decisions
- 11 States, 79 hospitals
- Data shared = data viewed
- Solves n=1 problem
Definitions of a high-quality pathway

• Expert driven
• Up-to-date
• Comprehensive
• Promotes participation in clinical trials
• Integrated, cost-effective technology & decision support
• Efficient processes for communication & adjudication
• Outcomes-driven results
• Promotes research and continuous quality improvement

American Society of Clinical Oncology Criteria for High-Quality Clinical Pathways in Oncology
Summary and Conclusions

• Precision cancer medicine is clinically available now

• Precision oncology requires a dedicated IT system, integrated with the EMR

• Healthcare IT trends are rapidly converging

• IT infrastructure for managing genomic data is absent at most institutions
Future Considerations

- True implementation of precision medicine requires outcomes measurement and a clinical champion.

- Emerging IT is quickly outpacing clinical adaptation (national EMR use = 75+%).

- Value-based care models will favor cost-saving technologies, such as precision medicine.

- Healthcare is hungry for tech innovations, but structurally flawed for implementation.
Thank you!

Lincoln Nadauld, MD, PhD
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Terence Rhodes, MD
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Ramya Thota, MD
Jonathan Hirsch