Clinical decision support in the era of genome informed cancer medicine

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Cancer Care Continuum

- Risk Assessment, Reduction & Screening
- Diagnosis
- Treatment Selection
- Treatment Plan Management
- Host & Disease Response Assessment
Biomarkers in the Cancer Care Continuum

- **Risk Assessment, Reduction & Screening**
  - **Risk Biomarker**: BRCA1/2

- **Diagnosis**
  - **Diagnostic Biomarker**: Estrogen Receptor

- **Treatment Selection**
  - **Prognostic Biomarkers**: OncotypeDx, Estrogen Receptor
  - **Predictive Biomarkers**: CYP2D6

- **Treatment Plan Management**
  - **Predictive Biomarkers**: Supportive Care Pharmacogenomics

- **Host & Disease Response Assessment**
  - **Response Biomarker**: Tumor Burden, Tumor Resistance, Host Toxicity
Decision Support
Cancer Care Continuum

Types of Decision Support:
- Which tests to order?
- How to interpret and report results?
- How to apply results to patient care?

Mode of Decision Support:
- When
- How
- To Whom
Unselected Population
2002
Comparison of 4 Chemotherapy Regimens in Advanced Lung Cancer

Schiller et al, NEJM ‘02

- Response rate – 19%
- Median TTP – 3.7 mos
- Median OS – 8 mos

1207 pts
Initial phase III first line EGFR TKI trial: “IPASS”
EGFR TKI vs. Carboplatin - Paclitaxel
in Never- or Light Ex-Smokers

Ref: Mok et al NEJM 2009; updated data Fukuouka et al JCO 2011
Unselected Population
Selected Population

Predictive Biomarker

Predict Treatment Efficacy

Informs Drug Selection
Treat Selected

Targeted Therapy

Primary Sensitivity

Disease Progress

Acquired Resistance

Primary Resistance
Riding the Tsunami of Genomic Data

Evolution of testing strategies
Single mutation -> Hot spot panels -> NGS
Levels of Evidence

Pre-clinical
- Animal Models
- Cell Lines
- Case Reports

Clinical Validity
- Retrospective Cohort Studies
- Non-randomized Prospective Studies

Clinical Utility
- Randomized Prospective Studies
- Guidelines

Separates one population into two or more groups with distinctly different outcomes

Incorporated into standard of care clinical decision making
## 2016

### Non-small cell lung cancer

<table>
<thead>
<tr>
<th>Molecular alteration</th>
<th>Drugs</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>EGFR mutation</td>
<td>erlotinib, gefitinib, afatinib</td>
<td>FDA approved</td>
</tr>
<tr>
<td>ALK rearrangements</td>
<td>crizotinib, ceritinib</td>
<td>FDA approved</td>
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<tr>
<td>EGFR T790M mutation</td>
<td>osimertrininib</td>
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<td>PD-L1 expression</td>
<td>pembrolizumab</td>
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<tr>
<td>BRAF mutation</td>
<td>Trametinib, dabrafenib</td>
<td>FDA approved</td>
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<td>ROS1 rearrangements</td>
<td>crizotinib</td>
<td>NCCN</td>
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<td>MET amplifications</td>
<td>crizotinib</td>
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<tr>
<td>HER2 mutations</td>
<td>trastuzumab, afatinib</td>
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</tr>
<tr>
<td>KRAS mutations</td>
<td>Resistance to TKI’s</td>
<td>NCCN</td>
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</tbody>
</table>
Mission of My Cancer Genome

To curate and disseminate knowledge regarding the clinical significance of genomic alterations in cancer
Manually Curated Content

21 Cancers

- ALL
- ALCL
- AML
- CML
- MDS
- GIST
- IMT
- Breast
- Glioma
- Gastric
- Lung
- Colorectal
- Basal Cell Carcinoma
- Bladder
- Medulloblastoma
- Melanoma
- Neuroblastoma
- Ovarian
- Rhabdomyosarcoma
- Thymic
- Thyroid

20 Pathways
823 Genes
21 Cancers
429 Variants
552 Drugs
**Map Kinase Pathway**

- **GF** to **RTK**
- **SRC** to **Kinase Domain**
- **SRC** to **SRC Inhibitors**
- **(H-/K-/N-) RAS**
- **RAF** and **RAF Inhibitors**
- **MEK1/2 (MAP2K1)**
- **MEK Inhibitors**
- **ERK1/2 (MAPK1)**
- **ERK Inhibitors**
- **Gene Transcription**
- **Nuclear Membrane**
- **Cell Growth and Survival**

**Inhibitors**

**21 Cancer Pathways**

**Associated Genes, Drugs, Diagnoses**
Find a Cancer Mutation

Disease (required): Select Disease

Gene (optional): Select Disease First

Variant (optional): Select Disease First

GO

Find Clinical Trials

Lists trials by Disease or Gene for all national and international trials registered within PDQ and clinicaltrials.gov.
Find a Cancer Mutation

Disease (required): 
- Select Disease
  - Acute Lymphoblastic Leukemia
  - Acute Myeloid Leukemia
  - Anaplastic Large Cell Lymphoma
  - Basal Cell Carcinoma
  - Bladder Cancer
  - Breast Cancer
  - Chronic Myeloid Leukemia
  - Colorectal Cancer
  - Gastric Cancer
  - GIST
  - Glioma
  - Inflammatory Myofibroblastic Tumor
  - Lung Cancer
  - Medulloblastoma
  - Melanoma
  - Myelodysplastic Syndromes
  - Neuroblastoma
  - Ovarian Cancer
  - Rhabdomyosarcoma
  - Thymic Carcinoma
  - Thyroid Cancer

Gene (optional):

Variant (optional):

Find Clinical Trials

Lists trials by Disease. More than 6000 trials registered on clinicaltrials.gov.
Find a Cancer Mutation

Disease (required): Lung Cancer

Gene (optional): Select Gene
- AKT1
- ALK
- BRAF
- DDR2
- EGFR
- FGFR1
- HER2
- KRAS
- MEK1
- MET
- NRAS
- NTRK1
- PIK3CA
- PTEN
- RET
- ROS1

Find Clinical Trials

Lists trials by Disease and Gene for all national and international trials registered within PDQ and clinicaltrials.gov.
Find a Cancer Mutation

Disease (required): Lung Cancer

Gene (optional): EGFR

Variant (optional): Select Variant
- EGFR Status Unknown
- EGFR No Mutation Detected
- EGFR c.2155G>C (G719A)
- EGFR c.2155G>T (G719C)
- EGFR c.2155G>A (G719S)
- EGFR Exon 19 Deletion
- EGFR Exon 19 Insertion
- EGFR Exon 20 Insertion
- EGFR c.2290-2291ins (A763_Y764insFQEA)
- EGFR c.2369G>T (T790M)
- EGFR c.2573T>G (L858R)
- EGFR c.2582T>A (L861Q)

Find Clinical Trials

Lists trials by Disease or Gene for all national and international trials registered within PDQ and clinicaltrials.gov.
Find a Cancer Mutation

Disease (required): Lung Cancer

Gene (optional): EGFR

Variant (optional): EGFR c.2369C>T (T790M)

GO

Find Clinical Trials

Lists trials by Disease or Gene for all national and international trials registered within PDQ and clinicaltrials.gov.
EGFR c.2369C>T (T790M) Mutation in Non-Small Cell Lung Cancer

**Location of Alteration in Gene**
- Kinase domain (exon 20)

**Levels of Evidence**
- FDA Approvals
- Guidelines
- Published clinical trial results
- Retrospective cohort analysis
- Case Reports
- Clinical trial eligibility criteria
- Pre-clinical studies

**Frequency of Alteration in Disease**
- 10% in the USA

**Response to Drug Sensitivity/Resistance**
- Currently no role for EGFR inhibitors

**Properties**
- Location of mutation: Keratin 5 domain (exon 20)
- Frequency of EGFR mutations in NSCLC: 10% in the USA
- EGFR mutant tumors with acquired resistance to gefitinib: Obayashi et al. 2005; Pao et al. 2005
- EGFR mutant tumors: Inukai et al. 2006

**What is EGFR?**
**EGFR in Lung Cancer**
**EGFR c.2369C>T (T790M)**
**Clinical Trials**
Dual inhibition of EGFR with afatinib and cetuximab in kinase inhibitor-resistant EGFR-mutant lung cancer with and without T790M mutations.


Abstract

EGFR-mutant lung cancers responsive to reversible EGFR inhibitors (gefitinib/erlotinib) develop acquired resistance, mediated by second-site EGFR T790M mutation in >50% of cases. Preclinically, afatinib (irreversible ErbB family blocker) plus cetuximab (anti-EGFR monoclonal antibody) overcomes T790M-mediated resistance. This phase Ib study combining afatinib and cetuximab enrolled heavily pretreated patients with advanced EGFR-mutant lung cancer and acquired resistance to erlotinib/gefitinib. Patients provided post-acquired-resistance tumor samples for profiling EGFR mutations. Among 126 patients, objective response rate (overall 29%) was comparable in T790M-positive and T790M-negative tumors (32% vs. 25%; P = 0.341). Median progression-free survival was 4.7 months (95% confidence interval, 4.3-6.4), and the median duration of confirmed objective response was 5.7 months (range, 1.8-24.4). Therapy-related grade 3/4 adverse events occurred in 44%/2% of patients. Afatinib-cetuximab demonstrated robust clinical activity and a manageable safety profile in EGFR-mutant lung cancers with acquired resistance to gefitinib or erlotinib, both with and without T790M mutations, warranting further investigation.

SIGNIFICANCE: This article reports the results of a trial combining afatinib and cetuximab in patients with acquired resistance and details the first clinical proof-of-concept for the preclinical hypothesis that a significant proportion of tumors in patients with acquired resistance to gefitinib/erlotinib remain dependent on EGFR signaling for survival.
Biomarker Classification & Prioritization

JCO, Levy 2013
Biomarker Representation

• Types of Biomarkers
  – Gene Variant (point mutations, insertions, deletions)
  – Exon
  – Fusions/Rearrangements
  – Gene Amplification
  – Protein Expression

• Logical Combinations of Alterations
  – AND/OR/NOT
Therapy Assertion
Lung Cancer & Erlotinib
(single alteration)

EGFR L858R mutation

Response: Primary Sensitivity
Line of Therapy: Metastatic
Therapy Assertions
Lung Cancer & Erlotinib
(co-occurring alterations)

- EGFR L858R mutation
- EGFR T790M mutation

Response: Acquired Resistance
Line of Therapy: Metastatic
Therapy Assertion
Colon Cancer & Cetuximab
(Alteration NOT detected in Variant Group)

Response: Primary Sensitivity
Line of Therapy: Metastatic
Source: FDA (KRAS Exon 2)
Source: NCCN (KRAS Exon 2, 3, 4)
Source: ASCO (KRAS Exon 2)
Prognostic Assertion
Acute Myeloid Leukemia
(single alteration)

Karyotype
Normal

Prognosis: Indeterminate
Source: NCCN
Prognostic Assertion

Acute Myeloid Leukemia
(co-occurring alterations)

Karyotype Normal

AND

NPM1 Exon 11 Mutation

Prognosis: Favorable
Source: NCCN
Prognostic Assertion
Acute Myeloid Leukemia
(co-occurring alterations)

Karyotype Normal
AND
NPM1 Exon 11 Mutation
AND
FLT3 ITD Detected

Prognosis: Unfavorable
Source: NCCN
Clinical Trial Annotation

Clinical Trial A

Arm 1
Arm 2
Arm 3
Arm n

Disease Group(s)
Include
Exclude

Biomarker Group(s)
Include
Exclude
Example: NCI Match

NCI Match

Arm G
Arm H
Arm U
Arm B
Arm R
Arm n

Disease Group(s)

Include:
- Solid Tumor
- Lymphoma

Exclude:
- Melanoma
- Colorectal & Papillary Thyroid Cancer

Biomarker Group(s)

Include:
- BRAF V600E/K/R/D Mutation

Exclude:
- KRAS, NRAS, HRAS mutations
## Curation: Disease & Biomarkers Criteria

### Linking Text in Primary Document to Annotation

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<th>Operator</th>
<th>Diseases</th>
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<tr>
<td>None</td>
<td>Colorectal Cancer (Disease), Melanoma (Disease), Papillary Thyroid Cancer (Disease)</td>
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</table>

**Add another Disease Criterion**

**Alterations**

<table>
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<tr>
<th>Alteration Operator</th>
<th>Alteration Criteria</th>
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</thead>
<tbody>
<tr>
<td>All</td>
<td>BRAF V600E, BRAF V600D, BRAF V600K, BRAF V600R</td>
</tr>
</tbody>
</table>

**Patients with a diagnosis of melanoma are excluded**

**Patients with a diagnosis of papillary thyroid cancer are excluded**

**Patients with a diagnosis of colorectal cancer are excluded**

**Patients must have a B-Raf proto-oncogene, serine/threonine kinase (BRAF) V600E or, V600K, V600R or V600D mutation** as identified via the NCI-MATCH Master Protocol.
Content Growth

- 86 genes
- 428 variants
- 968 diagnosis variant drug sensitivity (FDA)
- 1544 diagnosis variant drug sensitivity (experimental)
Contributor Network

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26 Institutions
10 Countries
4 Continents
Dissemination

Publically Available Resources
- Website
  - >2.5M page views, 201 countries
- Mobile App
  - >3634 Downloads, 22K sessions

Clinically Integrated Solutions
- Vanderbilt EHR
  - >5800 patients
- Laboratory Reporting Tool
  - >3200 specimens
What problem are you trying to solve?

Clinical Problem
Operational Problem
Informatics Problem
What Problem are you trying to solve?
Requirements for Success

- PEOPLE
- PROCESS
- TECHNOLOGY
Solution

- Tissue Specimen
- Workflow
- Communication
- Patient
- Physician
- Visualize Data
- Clinical Decision Support
- Data Acquisition
- Molecular Diagnostics Lab
<table>
<thead>
<tr>
<th>MR#</th>
<th>Patient Name</th>
<th>Actions</th>
<th>Tumor Gene Mutations</th>
<th>Result Status</th>
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<tr>
<td>03</td>
<td>74</td>
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</tbody>
</table>

Order Status (letter)
- O = Order Received
- R = Outside Specimen Requested
- A = Outside Specimen Arrived
- v = Specimen Accessioned

Result Status (colored box)
- Yellow = Gene Mutation Detected
- Grey = Gene Mutation Not Detected
- Red = No Result – Insufficient Specimen
New Method for Reporting Mutation Results in the EHR

Levy, ASCO 2011
Levy, Genome Research 2012
New Method for Reporting Mutation Results in the EHR

- Primary Sensitivity
- Primary Resistance
- Secondary Resistance

<table>
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</tr>
</thead>
<tbody>
<tr>
<td>03</td>
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<td>27 F, R M</td>
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<td>40 W, J E I</td>
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<tr>
<td>03</td>
<td>74 W, C L</td>
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</tr>
</tbody>
</table>

BRAF c.1798_1799GT>AG (V600R) Not Detected
BRAF c.1798_1799GT>AA (V600K) Not Detected
BRAF c.1799T>A (V600E) Detected
BRAF c.1799_1800TG>AA (V600E) Not Detected
BRAF c.1798G>A (V600M) Not Detected
BRAF c.1799T>G (V600G) Not Detected
BRAF c.1799_1800TG>AT (V600D) Not Detected

Levy, ASCO 2011
Levy, Genome Research 2012
Integrated, Individualized, and Intelligent Prescribing (I³P) Network

NHGRI IGNITE UO1

Co-Pl’s: Denny, Levy
I^3P Network

Aurora Health Care

Sanford Health

Vanderbilt University Medical Center

Meharry Medical College

Nashville General Hospital at Meharry

VA Health Care
DIAGNOSIS:

1. SKIN, LEFT POSTAURICULAR SCALP, SHAVE BIOPSY: FOCALLY INVASIVE WELL-DIFFERENTIATED SQUAMOUS CELL CARCINOMA, ARISING IN A BACKGROUND SQUAMOUS CELL CARCINOMA IN SITU, TRANSECTED AT BASE.

2. SKIN, LEFT NECK, SHAVE BIOPSY: INVASIVE WELL-DIFFERENTIATED SQUAMOUS CELL CARCINOMA, TRANSECTED AT BASE.

The attending pathologist electronically signed the report after examining and interpreting the slides/specimens with the resident.
Scale Reporting

1 Variant
1 Gene

40 Variants
6 Genes

1000s Variants
100s Genes

Next Generation Sequencing
Multi-modal testing

<table>
<thead>
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<td>74 W. C L</td>
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</table>

The epidermal growth factor receptor (EGFR) gene, mapped to 7p12, encodes a transmembrane glycoprotein that is a member of the protein kinase superfamily. EGFR protein is expressed on the cell surface and as a receptor binds to epidermal growth factor (EFG). The protein-ligand interaction induces receptor dimerization and tyrosine autophosphorylation resulting in cell proliferation. Somatic mutations in the tyrosine kinase-binding domain of the EGFR gene are associated with non-small cell lung carcinoma, primarily moderately to well-differentiated adenocarcinomas. EGFR mutations have been observed in approximately 10% of lung adenocarcinomas in the United States and are significantly associated with Asian ethnicity, female gender and never-smokers.

In summary, the results of this study demonstrate that this patient does not have an exon 19 deletion of the EGFR gene. The presence of this mutation indicates that this tumor is likely to be responsive to EGFR inhibitors. It is important to note that this assay is specific for these mutations and does not rule out the presence of other EGFR or ERBB2 mutations that may be present but not detected by this assay and which may affect treatment response.
**Approach**

Use MyCancerGenome as a Knowledge Base of clinically relevant variants for interpretation of NGS cancer panel.

- **Reference Sequence**
- **Known Variants Knowledge Bases**
  - **Sequence Alignment**
  - **Tumor/Normal Comparison Algorithm**
  - **Molecular Annotation of Variants**

**Classify clinical effect of variant(s)**

**Report Actionable Results & VUS**

**Variant-clinical effect knowledge bases**

**Clinical Decision**

*JCO, Levy 2013*
## Decision Support for Variant Analysis

### Actionable for Tumor Type

- **Gene:** EGFR
- **Position:** 7:55249071-55249071
- **G Change:** c.2309C>T
- **AA Change:** T790M
- **Mutation Type:** Substitution - Missense

### Actionable for Other Tumor Type

- **Gene:** EGFR
- **Position:** 7:55259515-55259515
- **G Change:** c.2573T>G
- **AA Change:** L858R
- **Mutation Type:** Substitution - Missense

### Not Actionable

<table>
<thead>
<tr>
<th>Variant Info</th>
<th>Ref:Alt</th>
<th>PGM Info</th>
<th>PGM Alignment</th>
<th>PGM Call</th>
<th>PGM Decision</th>
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<tbody>
<tr>
<td>Count: 0 Total (0 Confirmed)</td>
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</table>

- **Gene:** EGFR
- **Position:** 7:55249071-55249071
- **G Change:** c.2309C>T
- **AA Change:** T790M
- **Mutation Type:** Substitution - Missense

| Count: 0 Total (0 Confirmed) | | | | | |

- **Gene:** EGFR
- **Position:** 7:55259515-55259515
- **G Change:** c.2573T>G
- **AA Change:** L858R
- **Mutation Type:** Substitution - Missense

| Count: 0 Total (0 Confirmed) | | | | | |
### Decision Support for Variant Interpretation & Reporting

#### NGS RESULTS

**Detected Alterations With Therapeutic Implications**

<table>
<thead>
<tr>
<th>Gene</th>
<th>Alteration</th>
<th>Type of Mutation</th>
</tr>
</thead>
<tbody>
<tr>
<td>EGFR</td>
<td>T790M</td>
<td>Substitution - Missense</td>
</tr>
<tr>
<td>EGFR</td>
<td>L858R</td>
<td>Substitution - Missense</td>
</tr>
</tbody>
</table>

**Genes With Potentially Relevant Targeted Clinical Trials:** EGFR

**Genes With Other Non-Synonymous Alterations:** None

**Alterations that Failed Testing:** EGFR (L861Q)

#### Therapeutic Implications of Genomic Analysis, For Patient’s Tumor Type - Level 1

<table>
<thead>
<tr>
<th>Approved Drugs</th>
<th>Variants Detected</th>
<th>Response to Therapy</th>
<th>Condition</th>
<th>Line of Therapy</th>
<th>Level of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Afatinib</td>
<td>EGFR L858R, EGFR T790M</td>
<td>Acquired resistance</td>
<td>Non-Small Cell Lung Cancer; When resistance mutation occurs secondary to primary sensitizing mutation in EGFR</td>
<td>Metastatic</td>
<td>NCCN</td>
</tr>
<tr>
<td>Erlotinib</td>
<td>EGFR L858R, EGFR T790M</td>
<td>Acquired resistance</td>
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#### Potentially Relevant Targeted Clinical Trials - Level 3

(see note)

<table>
<thead>
<tr>
<th>Trial Title</th>
<th>Conditions</th>
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NGS RESULTS

Detected Alterations With Therapeutic Implications

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Therapeutic Implications of Genomic Analysis, For Patient's Tumor Type - Level 1

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<tr>
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### Decision Support for Variant Interpretation & Reporting

### NGS RESULTS

#### Detected Alterations With Therapeutic Implications

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#### Genes With Potentially Relevant Targeted Clinical Trials: EGFR

#### Genes With Other Non-Synonymous Alterations: None

#### Alterations that Failed Testing: EGFR (L861Q)

---

#### Therapeutic Implications of Genomic Analysis, For Patient's Tumor Type - Level 1

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### Potentially Relevant Targeted Clinical Trials - Level 3

**Trial Title**

- **Trial of Erlotinib and BKM120 in Patients With Advanced Non Small Cell Lung Cancer Previously Sensitive to Erlotinib (NCT01487265)**
  - Conditions: Non Small Cell Lung Cancer
  - Relevant Genes: EGFR

- **Phase II AZD9291 Open Label Study in NSCLC After Previous EGFR TKI Therapy in EGFR and T790M Mutation Positive Tumours (NCT02094261)**
  - Conditions: Non Small Cell Lung Cancer
  - Relevant Genes: EGFR

- **BATTLE-2 Program: A Biomarker-Integrated Targeted Therapy Study (NCT01248247)**
  - Conditions: Lung Cancer
  - Relevant Genes: EGFR

- **AZD9291 in Combination With Ascending Doses of Novel Therapeutics (NCT02143466)**
  - Conditions: Advanced Non Small Cell Lung Cancer
  - Relevant Genes: EGFR
Detected Alterations With Therapeutic Implications in Patient's Tumor Type - Level 1

Gene: EGFR
Nucleotide: c.2369C>T
Condition: Non-Small Cell Lung Cancer
Alteration Detected: T790M
Variation Type: Substitution - Missense

About this Gene
EGFR (epidermal growth factor receptor, also known as ERBB1 and HER1) is a gene that encodes for the epidermal growth factor receptor protein. Missense mutations, deletions, and insertions are observed in cancers such as lung cancer and glioblastoma. Activating EGFR mutations increase the kinase activity of EGFR, leading to hyperactivation of downstream pro-survival signaling pathways (Sordella et al. 2004).

Pathways
Receptor tyrosine kinase

Mutation Location in Gene and/or Protein
Kinase domain (exon 20)

Mutation Prevalence
Frequency of EGFR mutations in NSCLC: 10% in the USA and 35% in Asia (Lynch et al. 2004)

Frequency of T790M mutations in EGFR-mutated NSCLC: < 5% of untreated EGFR mutant tumors (Inukai et al. 2006); 50% of EGFR mutant tumors with acquired resistance to erlotinib/gefitinib (Kobayashi et al. 2005; Pao et al. 2005)

Response to Drugs
Response to anti-EGFR antibodies: Currently no role for EGFR mutation in predicting response in NSCLC
Response to EGFR TKIs: Confers decreased sensitivity

Reference
http://www.mycancergenome.org/content/disease/lung-cancer/egfr/4

Content from My Cancer Genome

Link to MyCancerGenome.org
Trial Matching Decision Support

NCI Match 21 trial arms

861 cases with NGS testing at Vanderbilt

36% potential match

Next Steps: Extend trial annotation & integrate algorithm into clinical workflow
Challenges & Future Directions

My Cancer Genome

Content Generation ➔ Content Dissemination
Small Sub-populations

Targeted Therapy

Primary Sensitivity

Primary Resistance

Acquired Resistance
Only 5% of cancer patients participate in clinical trials
Learning Cancer System
Learning Cancer System

Outcomes

Population Analysis

Treatment Selection
83% of US physicians have EHR System

Adoption of EHRs by US Physicians

Office of the National Coordinator:
EHR Data Created Each Year at Vanderbilt

7M Clinical Notes

9M Scanned Image Pages

5M Lab Orders

8M Medications Dispensed

15M Clinical Communications

1.6M Vital Signs

1.7M Outpatient Prescriptions

55K hospital discharges

1.9M ambulatory visits
190M Nursing Data Elements
WHAT LIES BENEATH?
A COMPARISON OF CLAIMS DATA AND EHR DATA AVAILABLE FOR 500 PATIENTS

CLAIMS DATA
The foundation for most healthcare analytics, Claims Data is easy to come by, but delayed, and short on details.

EHR DATA
Real-time, rich in clinical content, and right under your fingertips. EHR data enhances risk algorithms and informs outcomes-based measures.

© 2015 Arcadia Solutions
5686 Hospitals
25K Clinics
10K Reference Labs
23K Pharmacies
State & Federal Health Agencies
50 Health Insurance Payors
Health Information Exchange
2.5 Quintrillion bytes of data are created everyday

90% of the data in the world today has been created in the last two years alone

-Big Data Beyond the Hype
Vanderbilt’s De-identified Synthetic Derivative of EHR Linked to Germ line DNA biobank (BioVU) and pathology tissue library

Advantages of BioVU

- **2.5 M** Number of patient records accessible in Synthetic Derivative – the largest database of its kind
- **211,000** Number of clinical records that have matching genetic data (75k already genotyped)

Patient Records

- **27K** Breast Cancer ICD code
- **6.6K** Tumor Registry Data
- **4K** germ line DNA samples
- **5.7K** tumor specimens

Novel Methods

- **180** Peer-reviewed publications in the last 7 years from VUMC researchers creating / validating methodologies

Amount Invested

- **$12 M** Investment to create BioVU over the last 10 years

Genetic Data

Jill Pulley
Many Are Looking at Different Parts of the Same Problem
President Obama’s State of the Union Address pushes for precision medicine

- 2015 – 1 Million person precision medicine cohort
- 2016 – Moonshot to “cure” cancer (Biden named “Cancer Czar”)
THERE ARE TWO KINDS OF PEOPLE:

1) THOSE THAT CAN EXTRAPOLATE FROM INCOMPLETE DATA.
Complex Cancer Treatment Pathways

Ravi Atreya
Evolution of Clinical Decision Support

- Evidence Driven
- Protocol Driven
- Pathway Driven
- Data Driven?


If You Can't Measure It, You Can't Improve It

(William Thomson, Lord Kelvin)
AND WARREN HERE IS IN CHARGE OF OUR GUT FEELINGS
Data fluency: the ability to use the language of data to fluidly exchange and explore ideas within an organization

Gemignani, Gemignani, “Data Fluency: Empowering Your Organization with Effective Data Communication” 2014
Summary

• Rise of genomic profiling in cancer
• My Cancer Genome knowledge base provides decision support for clinical utility of alterations in cancer
• Strategies for content generation and dissemination
• Strategies for clinical decision support
## Acknowledgements

<table>
<thead>
<tr>
<th>Mia Levy</th>
<th>Lucy Wang</th>
<th>Tracy Shields</th>
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<td>Christine Lovly</td>
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<tr>
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<td>Nunzia Giuse</td>
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</tr>
<tr>
<td>Kate Mittendorf</td>
<td>Taneya Koonce</td>
<td>And many more…</td>
</tr>
<tr>
<td>Scott Sobecki</td>
<td>Sheila Kusnoor</td>
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<tr>
<td>Joey Schneider</td>
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<td>Melissa Stamm</td>
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Thank You

mia.levy@vanderbilt.edu