National Cancer Policy Forum Workshop
November 10, 2014

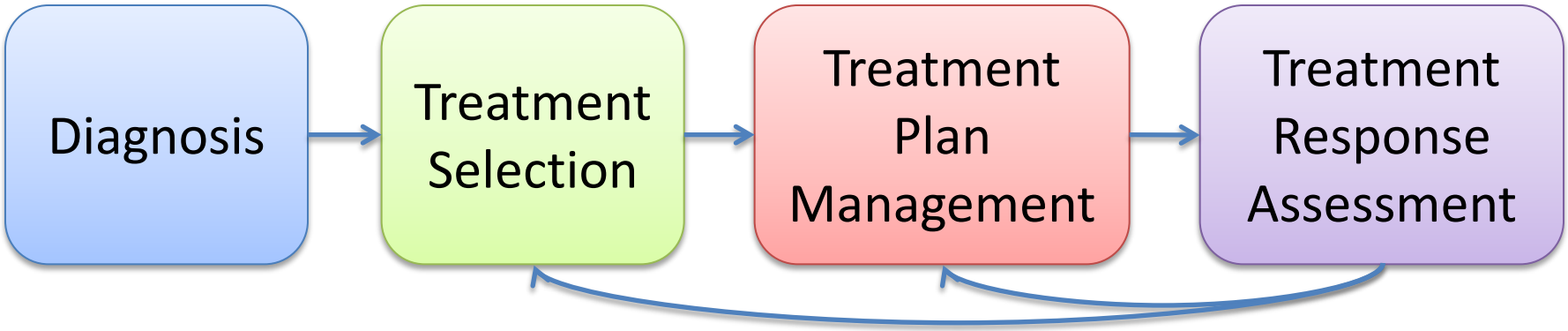
New challenges with next generation sequencing

Mia Levy, MD, PhD
Vanderbilt Ingram Cancer Center

Disclosures

- GenomOncology – Consulting
- Personalis - Consulting

Biomarkers for decision support in the continuum of cancer care



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

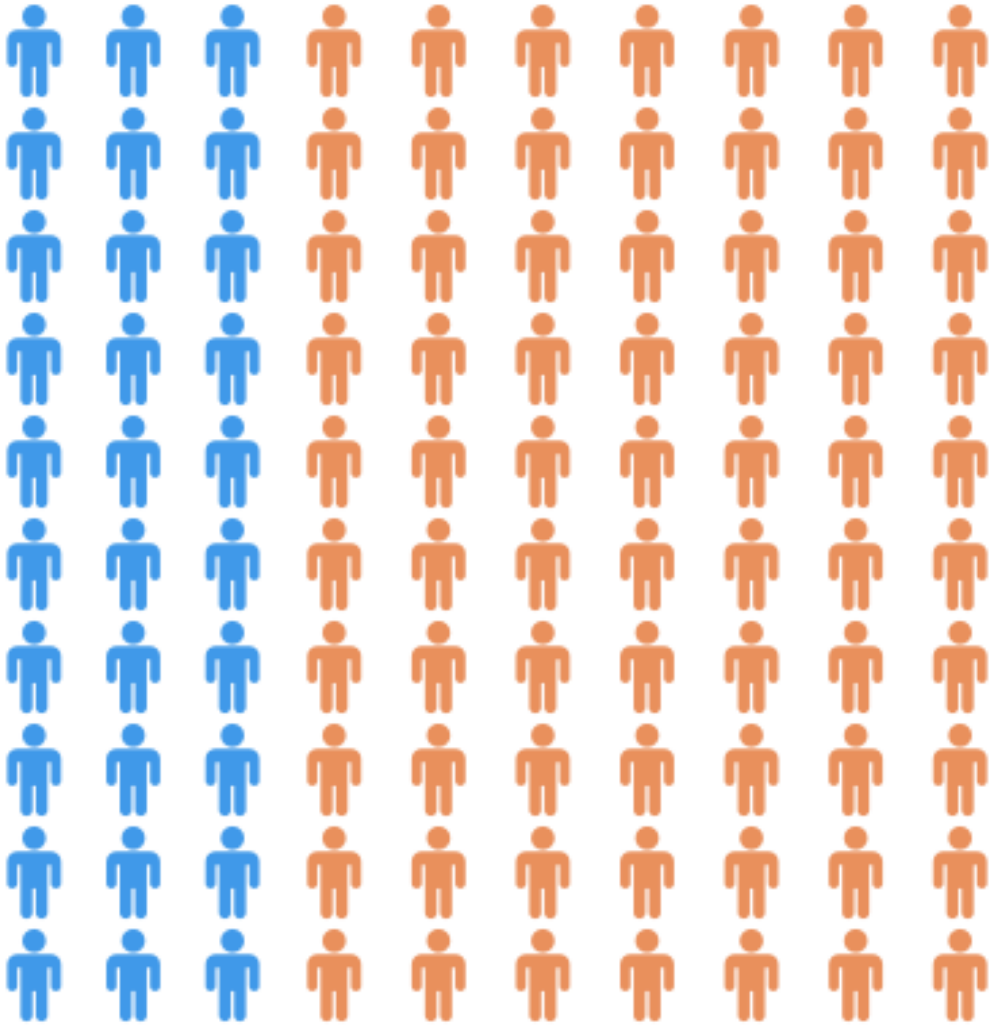
How

To Whom

Unselected Population

Treat Unselected

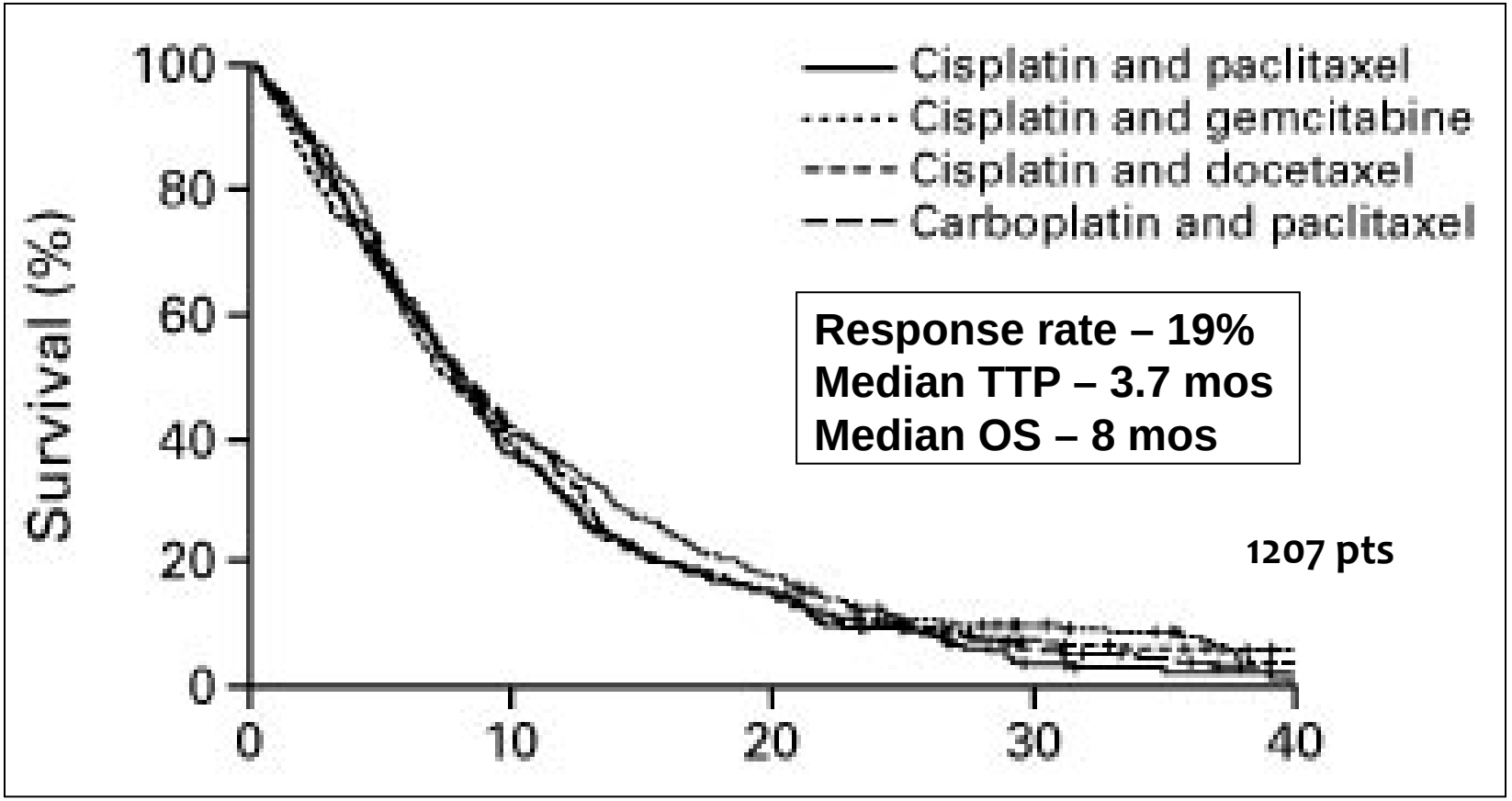
Response



No Response

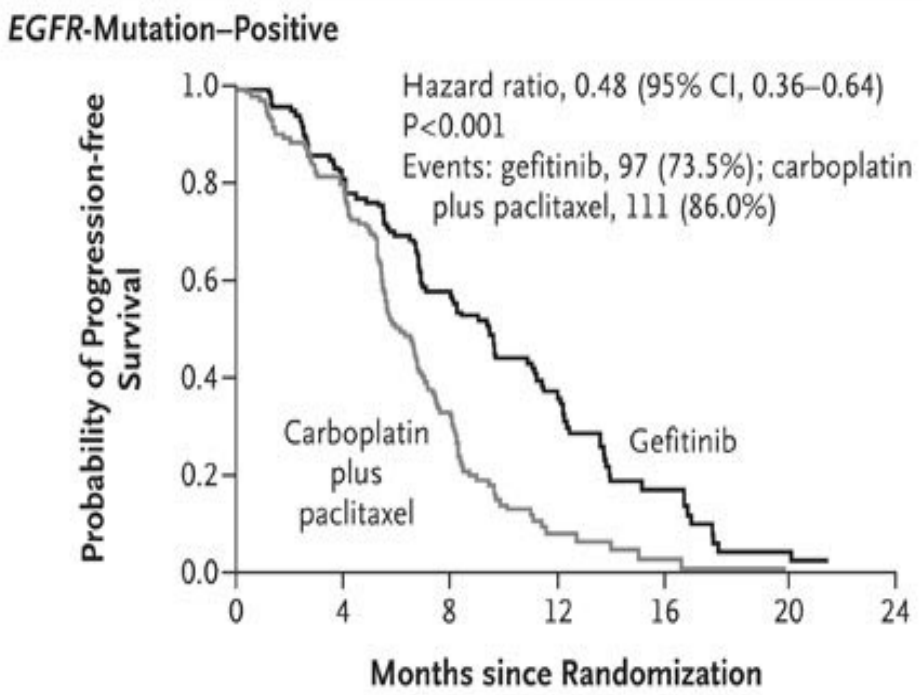
2002

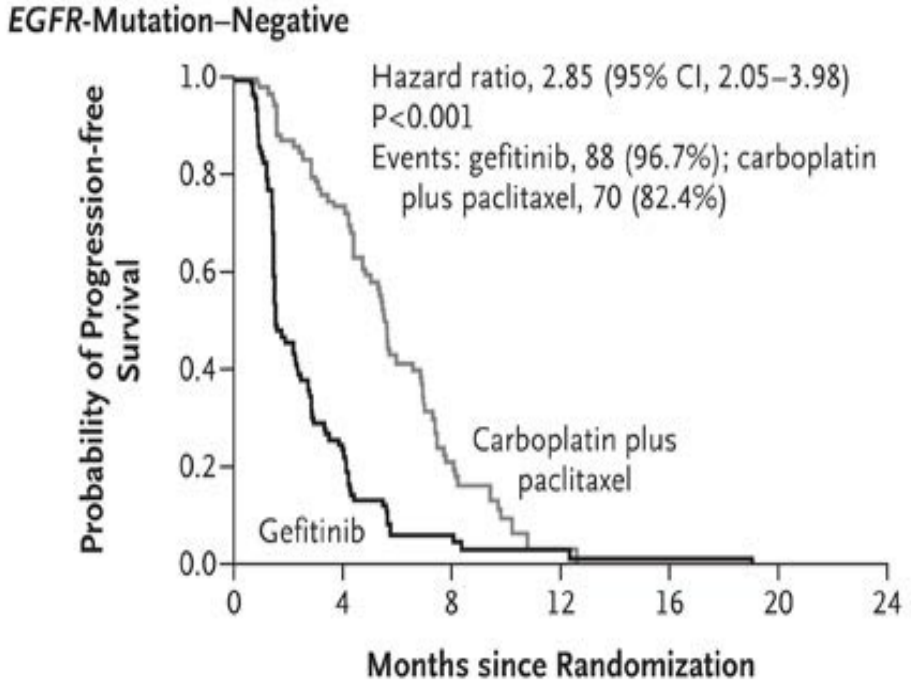
Comparison of 4 Chemotherapy Regimens in Advanced Lung Cancer



Schiller et al, *NEJM* '02

2009
EGFR mutated lung cancer



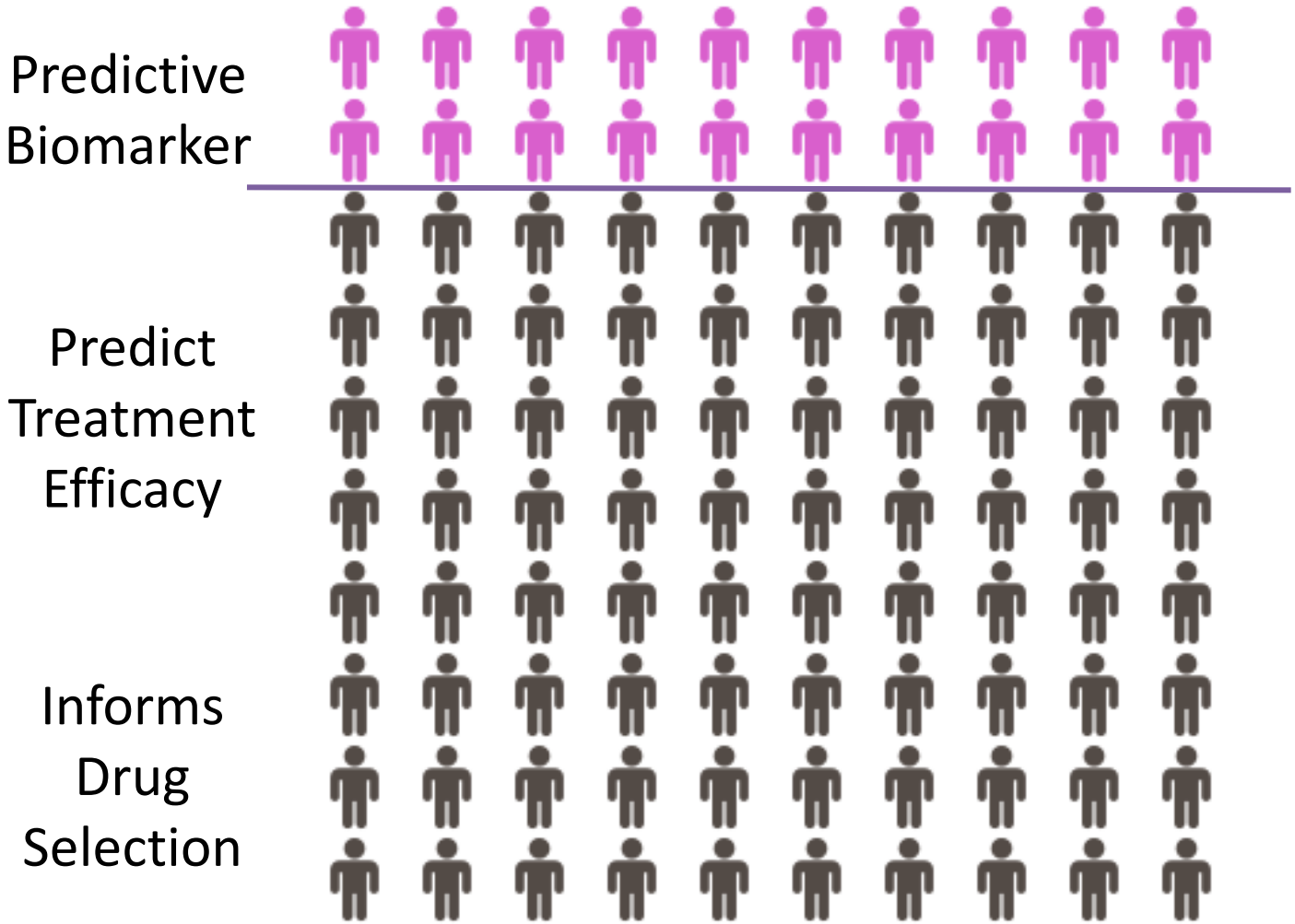


Initial phase III first line EGFR TKI trial: "IPASS"
EGFR TKI vs. Carboplatin - Paclitaxel
in Never- or Light Ex-Smokers

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

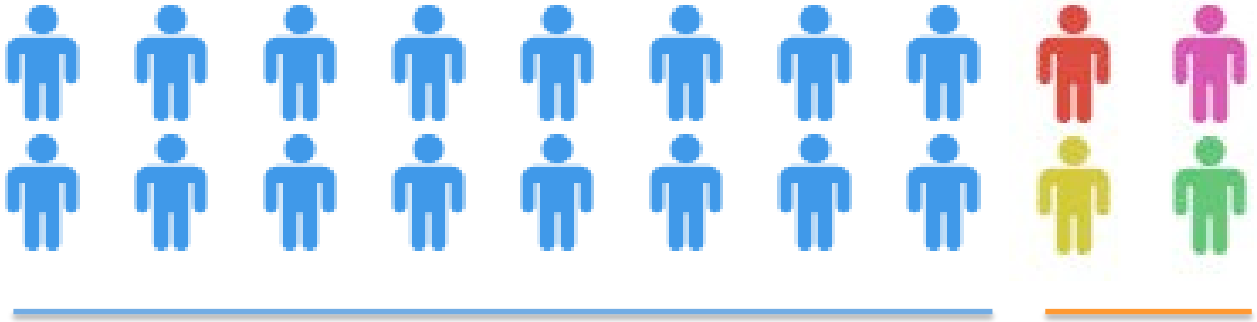
Unselected Population

Selected Population



Treat Selected

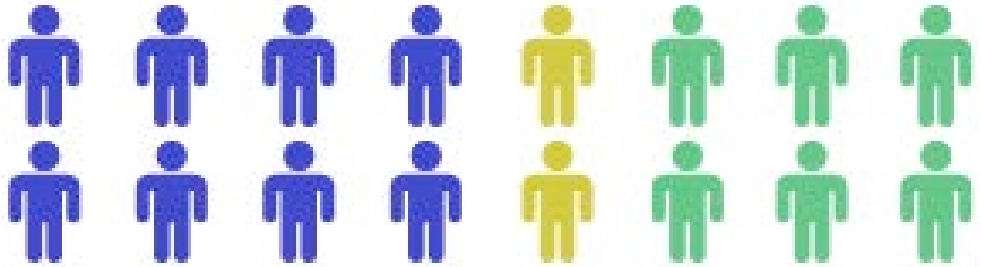
Targeted Therapy



Primary Sensitivity

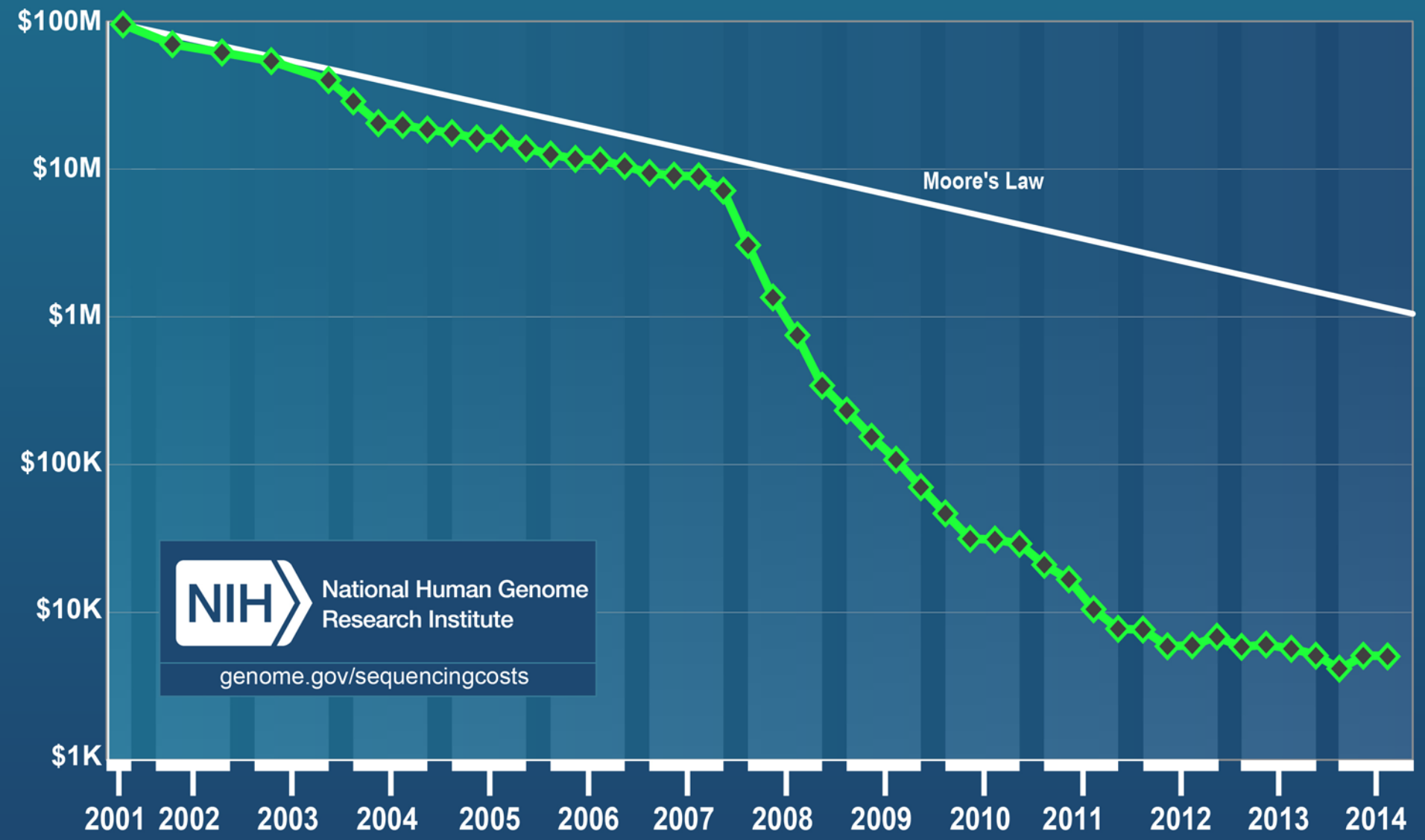
Primary Resistance

Disease Progress



Acquired Resistance

Cost per Genome



http://www.genome.gov/sequencingcosts/

Riding the Tsunami of Genomic Data

Evolution of testing strategies

Single mutation -> Hot spot panels -> NGS

Knowledge Gap

Surveys Reveal Wide Gaps in Knowledge of Genetic Mutation Testing Exist Between Oncologists, Nurses and Cancer Patients

RIDGEFIELD, Conn., Nov. 16, 2011 /PRNewswire/ -- Despite guidelines calling for genetic mutation testing in certain patients with lung cancer, three new surveys fielded by Harris Interactive reveal a disconnect in the understanding of and communication about genetic mutation testing among healthcare professionals and cancer patients. Results of the surveys were announced today by Boehringer Ingelheim Pharmaceuticals, Inc., which sponsored the surveys in partnership with the Association of Community Cancer Centers (ACCC), ONS:Edge and the National Lung Cancer Partnership (NLCP).

Surveys of 95 comm in October 2011 to measure per h.

Cancer researchers rmally and form cancers, includ informed treatment decisions, ce has not been widely adopted

The surveys found t ents, only 17 percent of lung canc percent) did not discuss genetic mutation testing with patients, primarily because they felt that they lacked the knowledge to discuss it (56 percent) or didn't have the proper resources to share with their patients (33 percent). These findings highlight the need for a greater understanding of genetic mutation testing.

> "Three new surveys… reveal a disconnect in the understanding of and communication about genetic mutation testing among healthcare professionals and cancer patients"

Levels of Evidence

Animal Models

Cell Lines

Case Reports

Retrospective Cohort Studies

Non-randomized Prospective Studies

Guidelines

Randomized Prospective Studies

Pre-clinical

Clinical Validity

Clinical Utility

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

Incorporated into standard of care clinical decision making

Old Method for Reporting Mutation Results in the Electronic Medical Record

Old Method:

- Report Template
- Scanned into Electronic Health Record as image file (not computable)

Challenges:

- How to report > 100's genes?
- Whose role to curate knowledge regarding clinical significance?
- Lack clinical trial information

Name: **Sex:** **Laboratory Number:** **VUH#:**

Referral Source:

Reason for Request: DNA Analysis for *EGFR* Mutations

Type of Specimen: _____ (Block #_____)

Date Received:

Date of Report:

Interpretation: ***EGFR* Mutation Detected: Exon 19 deletion**

EGFR Mutations Tested Include:
Exon 19 deletion, Exon 21 (L858R), Exon 20 insertion

ERBB2 Mutation Tested:
Exon 20 insertion

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 (EGF). 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 adenocarcinoma. *EGFR* mutations have been observed in approximately 10% of lung adenocarcinomas in patients from the United States and are significantly associated with Asian ethnicity, female gender and never-smokers.

ERBB2 is a member of the EGF family of receptor tyrosine kinases and plays important roles in the pathogenesis of several human cancers. Somatic mutations in the form of in-frame duplications and/or insertions in a small stretch of exon 20 have been reported in non-small cell lung carcinomas. Of interest, exon 20 insertion mutations in *ERBB2* or *EGFR* are significantly more prevalent in the same subpopulations in which other *EGFR* mutations occur.

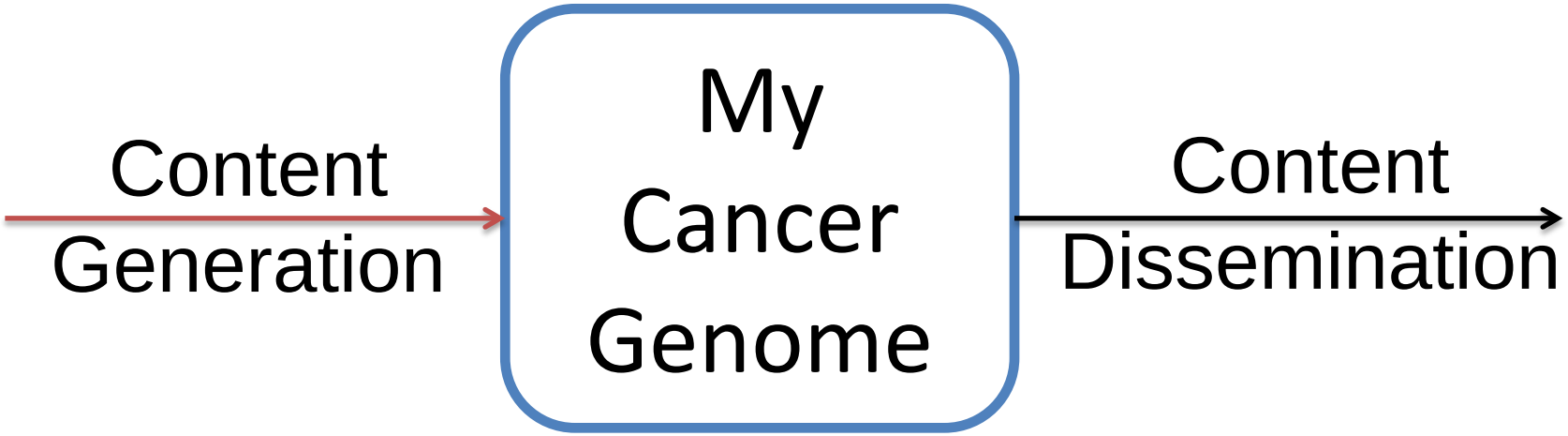
Progressive and/or metastatic non-small cell lung carcinomas can be treated with inhibitors of the EGFR receptor. Somatic mutations in the tyrosine kinase domain of the *EGFR* gene present in lung adenocarcinomas can affect a patient's response to EGFR inhibitors. 90% of *EGFR* mutations in this population include short in-frame deletions in exon 19 and a T > G point mutation in exon 21 at codon 858 (L858R). The presence of either mutation correlates with sensitivity to EGFR inhibitors. Conversely, insertion mutations in exon 20 of either *ERBB2* or *EGFR* gene appear to be less responsive to therapy.

DNA extracted from this patient's tumor was amplified for *EGFR* exons 19 and 20 and *ERBB2* exon 20 using multiplex fluorescent PCR to detect small deletions or insertions. Detection of mutation L858R was performed using fluorescent PCR coupled with restriction endonuclease digestion with *Sau*96I. All amplicons were analyzed using capillary electrophoresis. An in frame deletion in exon 19 of the *EGFR* gene was detected.

In summary, the results of this study demonstrate that this patient does have an exon 19 deletion of the *EGFR* gene. The presence of this mutation indicates that this tumor will likely be responsive to EGFR inhibitors. It is importatnt to note that this assay is specific for these four 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.

Mission of My Cancer Genome

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


Content
Generation
My
Cancer
Genome
Content
Dissemination

Find a Cancer Mutation

Disease (required): Select Disease

Gene (optional):

Variant (optional):

GO

Find Clinical Trials

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

Disease (optional): Enter a Disease

Gene (optional): Enter a Gene

GO

Learn About My Cancer Genome

Support My Cancer Genome

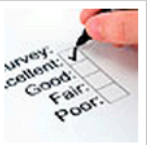
Help create new tools and resources

More...

Molecular Medicine

- Articles of Interest
- List of Targeted Therapies
- Overview on Targeted Therapies for Cancer
- How Gene Alterations are Detected

Feedback



Take our Survey and help us improve our service

More...

My Cancer Genome

Genetically Informed Cancer Medicine

Search My Cancer Genome

Go

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Gene (optional):

Variant (optional):

GO

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GO

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

56 Genes

428 Disease-Gene-Variant Relationships

What is EGFR? | EGFR in Lung Cancer | EGFR c.2369C>T (T790M) | Clinical Trials

EGFR c.2369C>T (T790M) Mutation in Non-Small Cell Lung Cancer

Properties	
Location of mutation	Kinase domain (exon 20)
Frequ…	…USA
	…Paez et al. 2004; Pao et al. 2004)
R…	…*GFR* mutant tumors (Inukai et al. 2006)
n…	…nt tumors with acquired resistance to
	…obayashi et al. 2005; Pao et al. 2005)
I…	
R…	…sensitivity
(…	
R…	…sensitivity
(…	
R…	…sensitivity
EG…	
Response to anti-EGFR antibodies	Currently no role for *EGFR*

Location of Alteration in Gene

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

Response to Drug Sensitivity/Resistance

MY CANCER GENOME
GENETICALLY INFORMED CANCER MEDICINE

Search My Cancer Genome | Go

Home | DIRECT | About Us

Find a Cancer Mutation

Disease (required): Select Disease

Gene (optional):

Variant (optional):

GO

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Gene (optional): Enter a Gene

GO

Clinical trial search
> 40K Cancer Trials (PDQ)
135 Cancer Diagnoses
500+ Cancer Genes

Learn About My Cancer Genome

Support My Cancer Genome

Help create new tools and resources

Feedback

Take our Survey and help us improve our service

More...

MY CANCER GENOME
GENETICALLY INFORMED CANCER MEDICINE

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Find a Cancer Mutation

Disease (required): Select Disease

Gene (optional):

Find

Gene (optional): Enter a Gene

GO

Cancer Drug-Targets (>500 drugs)

- Targeted therapeutics
  - Tyrosine Kinase Inhibitors
  - Monoclonal Antibodies
- Immunotherapy
- Hormone therapy
- Cytotoxic chemotherapy

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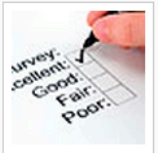
Feedback



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My Cancer Genome

Genetically Informed Cancer Medicine

Search My Cancer Genome

Go

Home | DIRECT | About Us

DIRECT

- Rare mutation database
- Published case reports of drug response

Find a Cancer

Disease (require

Gene (optional):

Variant (optional):

GO

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Disease (optional): Enter a Disease

Gene (optional): Enter a Gene

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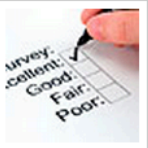

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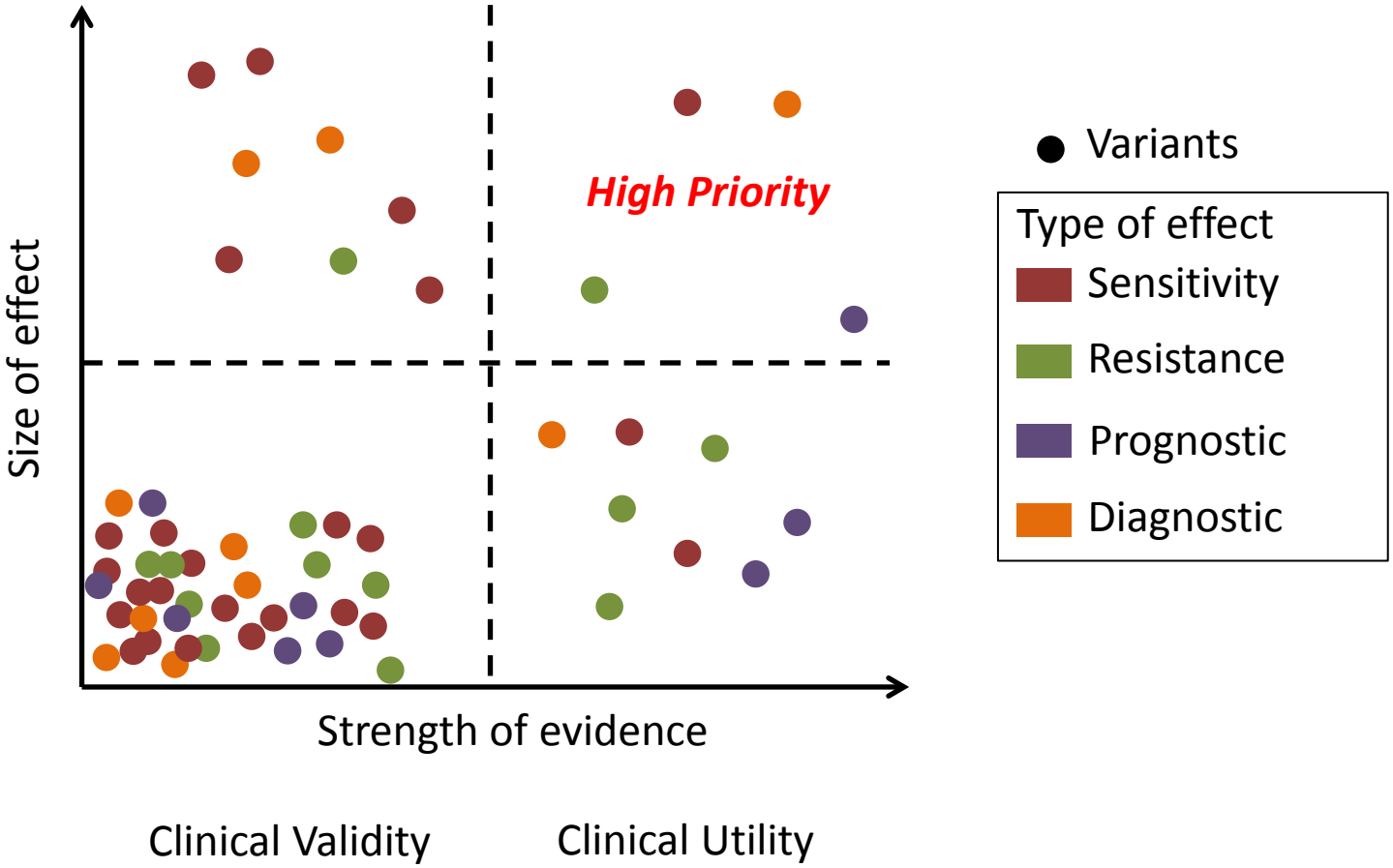
More...

Biomarker Classification & Prioritization



JCO, Levy 2013

Biomarker Representation

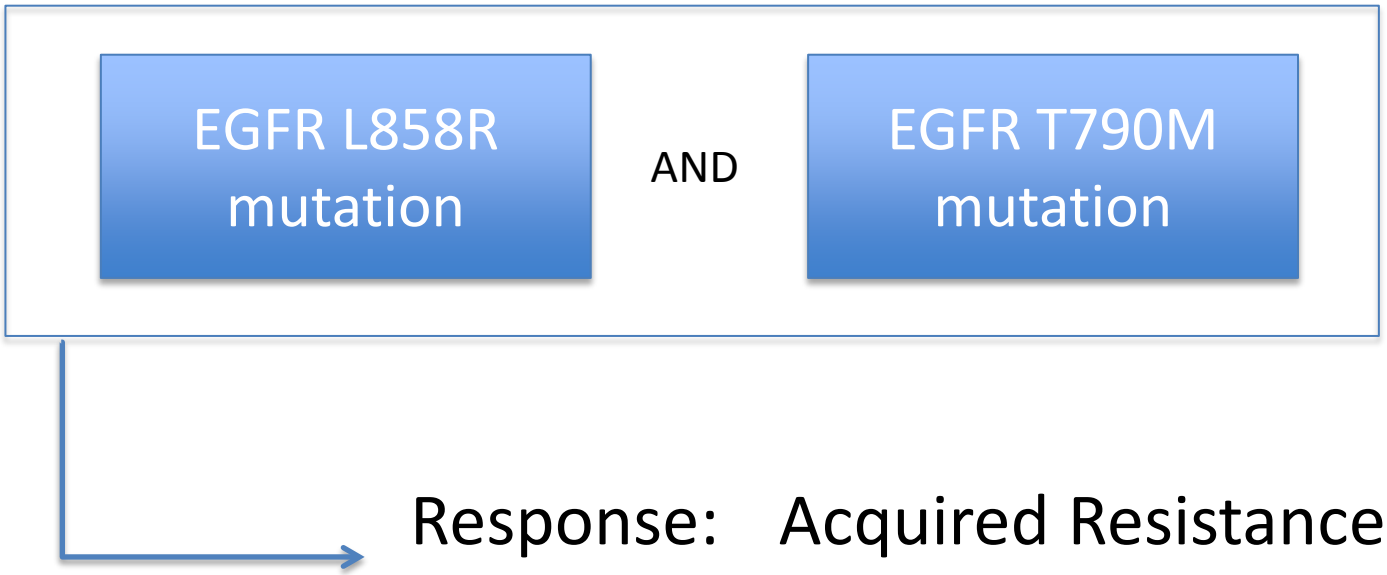
- **Types of Biomarkers**
  - Gene Variant (point mutations, insertions, deletions)
  - Exon
  - Fusions/Rearrangements
  - Gene Amplification
  - Protein Expression
- **Logical Combinations of Alterations**
  - AND/OR/NOT

Example: Lung Cancer & Erlotinib

(single alteration)

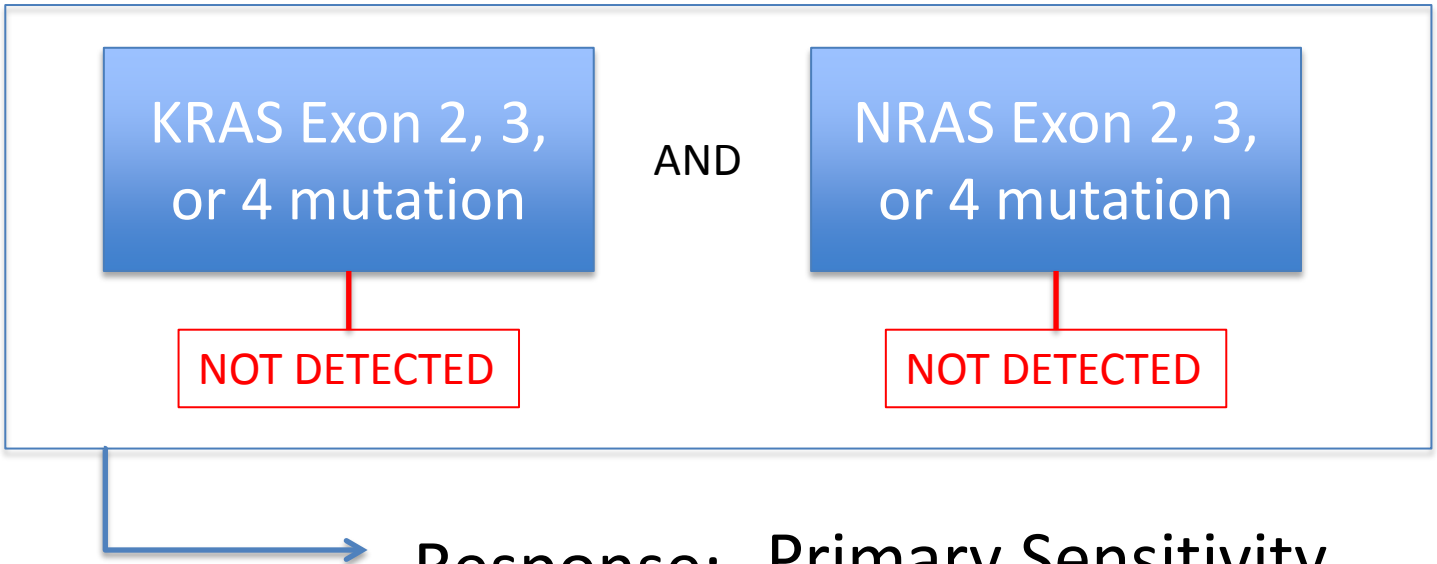
Example: Lung Cancer & Erlotinib

(co-occuring alterations)

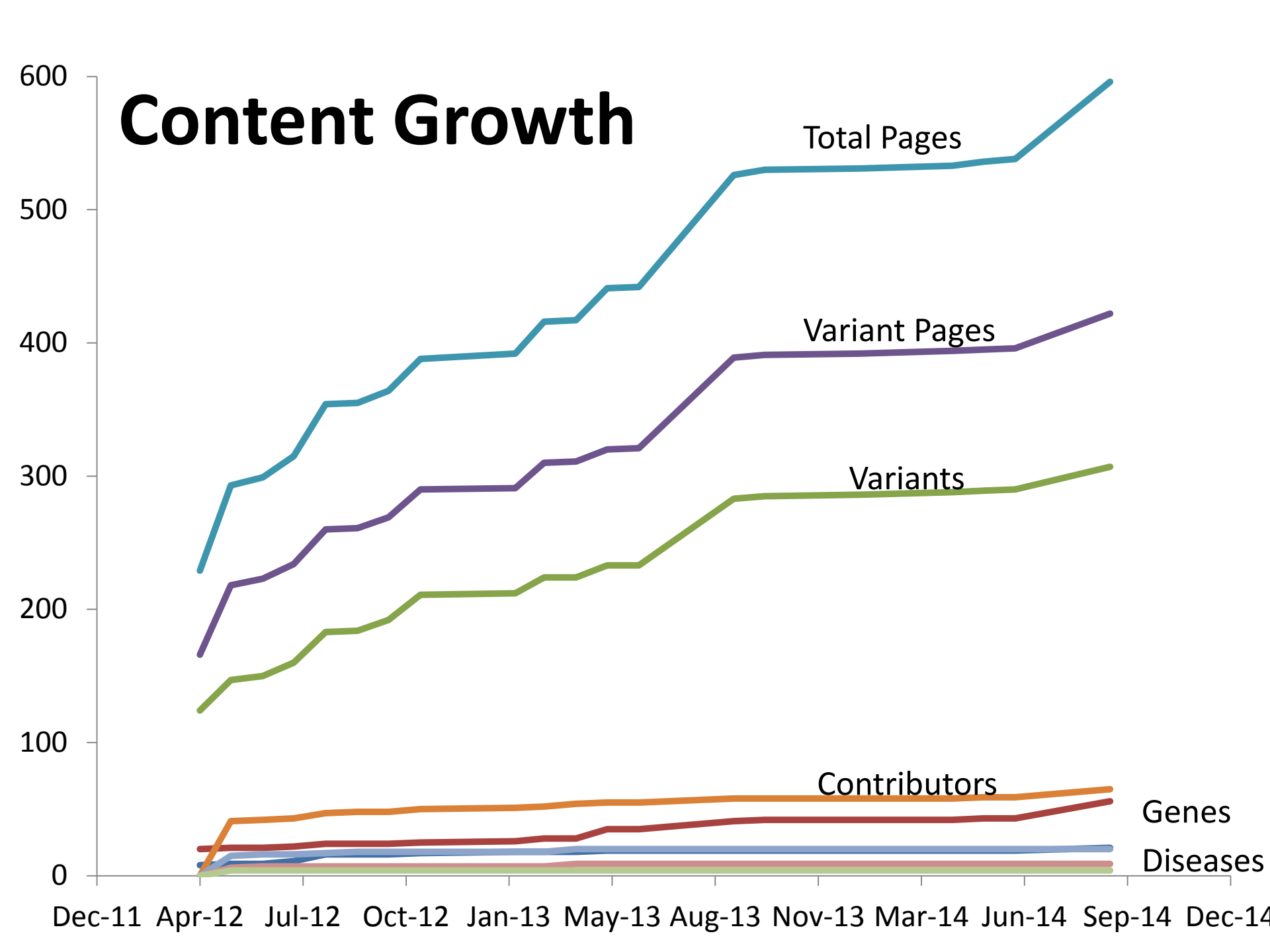


Example: Colon Cancer & Cetuximab

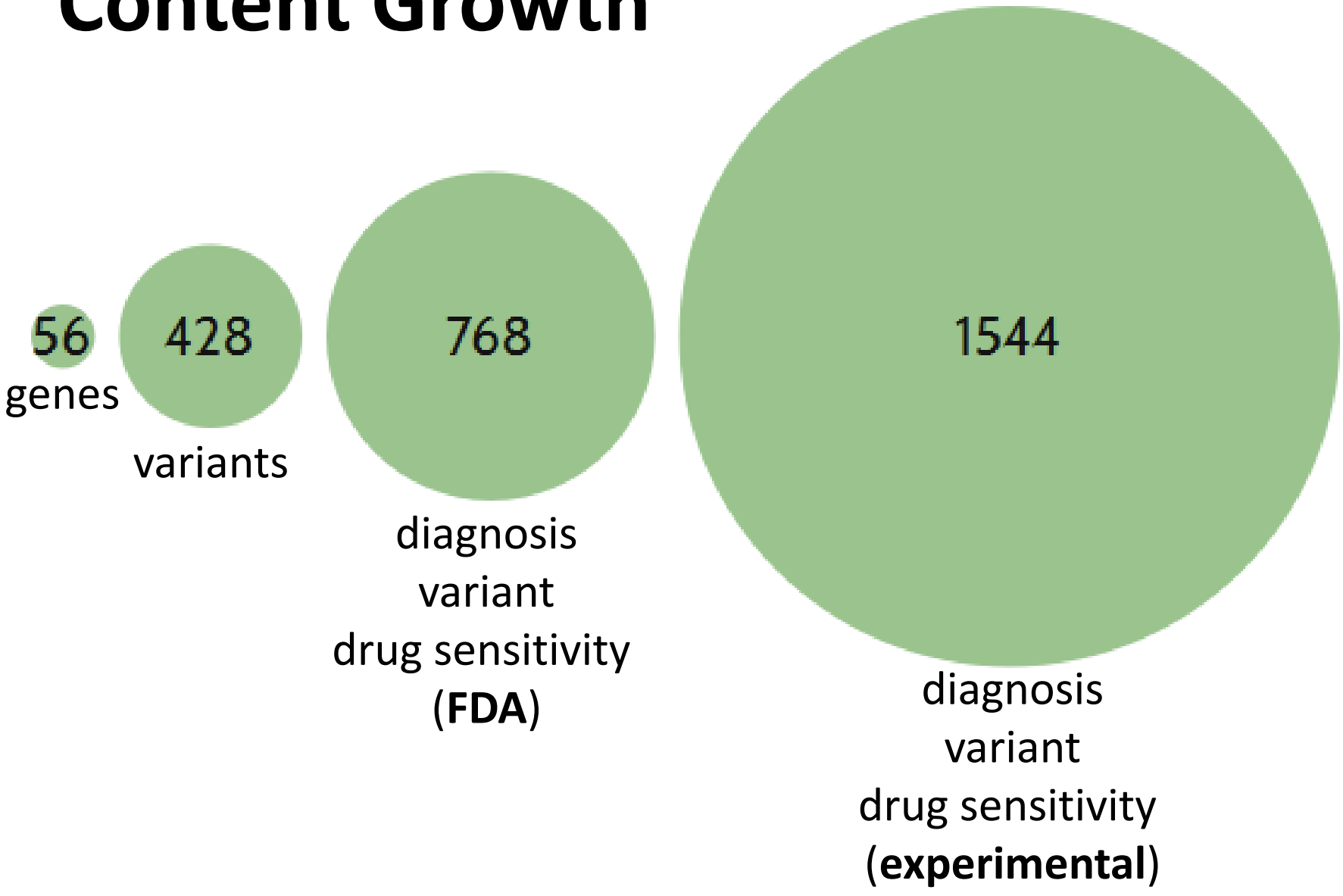
(Alteration NOT detected in Variant Group)



Response: Primary Sensitivity
Line of Therapy: Metastatic
Source: FDA (KRAS Exon 2)
Source: NCCN (KRAS Exon 2, 3, 4)
Source: ASCO (KRAS Exon 2)

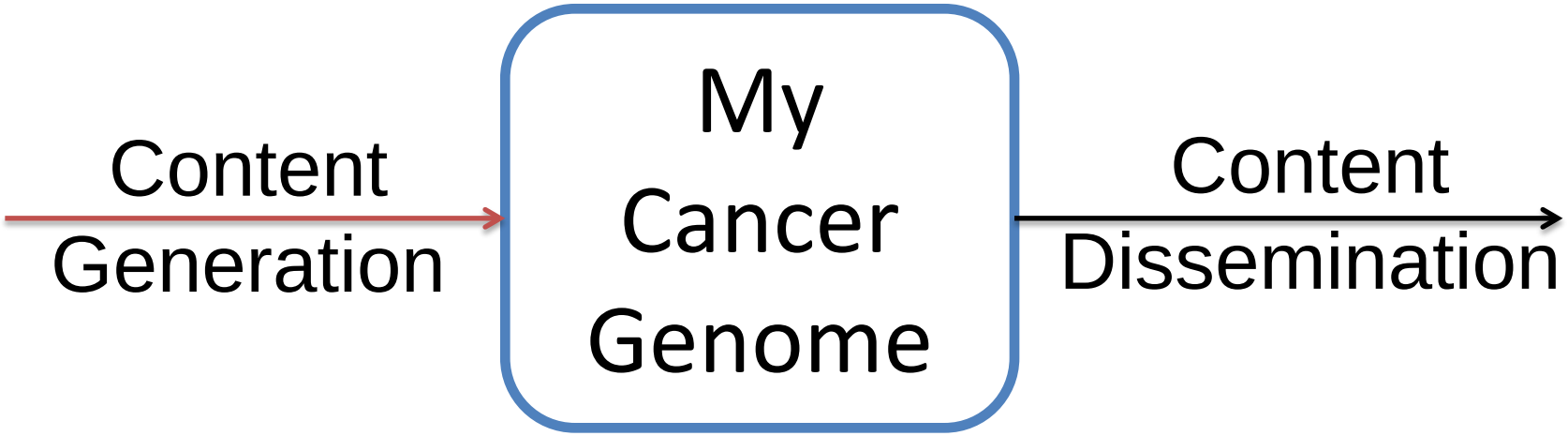

Content Growth
Total Pages
Variant Pages
Variants
Contributors
Genes
Diseases
600
500
400
300
200
100
0
Dec-11
Apr-12
Jul-12
Oct-12
Jan-13
May-13
Aug-13
Nov-13
Mar-14
Jun-14
Sep-14
Dec-14

Content Growth



Contributor Network

Worldwide Collaboration


Content
Generation
My
Cancer
Genome
Content
Dissemination

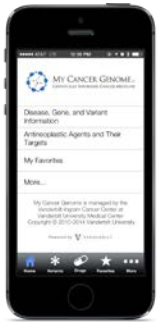
Dissemination

Publically Available Resources

Clinically Integrated Solutions

Website

>5,700 site visits per week



Mobile App

>1100 Downloads

My Cancer Genome

Vanderbilt EHR

Laboratory Reporting Tool

GenomOncology
BATTLING CANCER, ONE GENOME AT A TIME

New Method for Reporting Mutation Results in the EHR

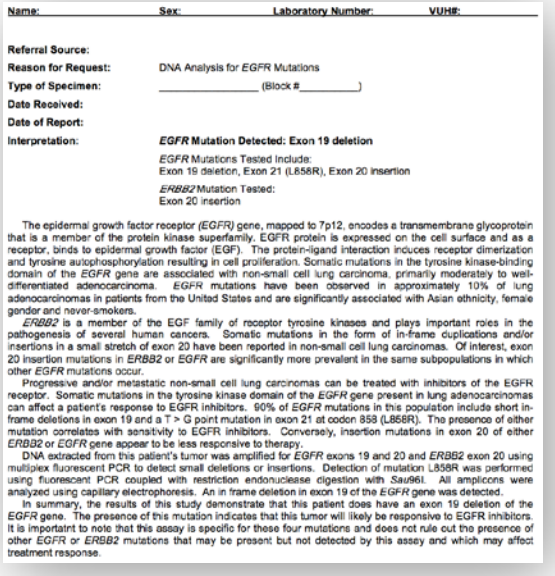
MR#	Patient Name	Actions	Tumor Gene Mutations						
			H-SMP	BRAF	CTNNB1	GNA11	GNAQ	KIT	NRAS
03 81	A, B M.	Actions	■	■					
03 56	A, P	Actions	■		■				■
03 35	B, J A	Actions	■						■
01 80	B, S A	Actions							
02 29	E, J E	Actions	■					■	
02 27	F, R M	Actions							
02 77	G, T	Actions							
02 73	H, A	Actions	■			■			
03 64	S, C	Actions	A						
02 79	S, A S	Actions	R						
02 40	W, J E I	Actions							
03 74	W, C L	Actions	■	■					

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

Scale Reporting

1 Variant
1 Gene



Name: **Sex:** **Laboratory Number:** **VUH#:**

Referral Source:
Reason for Request: DNA Analysis for *EGFR* Mutations
Type of Specimen: _____ (Block #_____)
Date Received:
Date of Report:
Interpretation: ***EGFR* Mutation Detected: Exon 19 deletion**

EGFR Mutations Tested Include:
Exon 19 deletion, Exon 21 (L858R), Exon 20 insertion

ERBB2 Mutation Tested:
Exon 20 insertion

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 (EGF). 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 adenocarcinoma. *EGFR* mutations have been observed in approximately 10% of lung adenocarcinomas in patients from the United States and are significantly associated with Asian ethnicity, female gender and never-smokers.

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DNA extracted from this patient's tumor was amplified for *EGFR* exons 19 and 20 and *ERBB2* exon 20 using multiplex fluorescent PCR to detect small deletions or insertions. Detection of mutation L858R was performed using fluorescent PCR coupled with restriction endonuclease digestion with *Sau*96I. All amplicons were analyzed using capillary electrophoresis. An in frame deletion in exon 19 of the *EGFR* gene was detected.

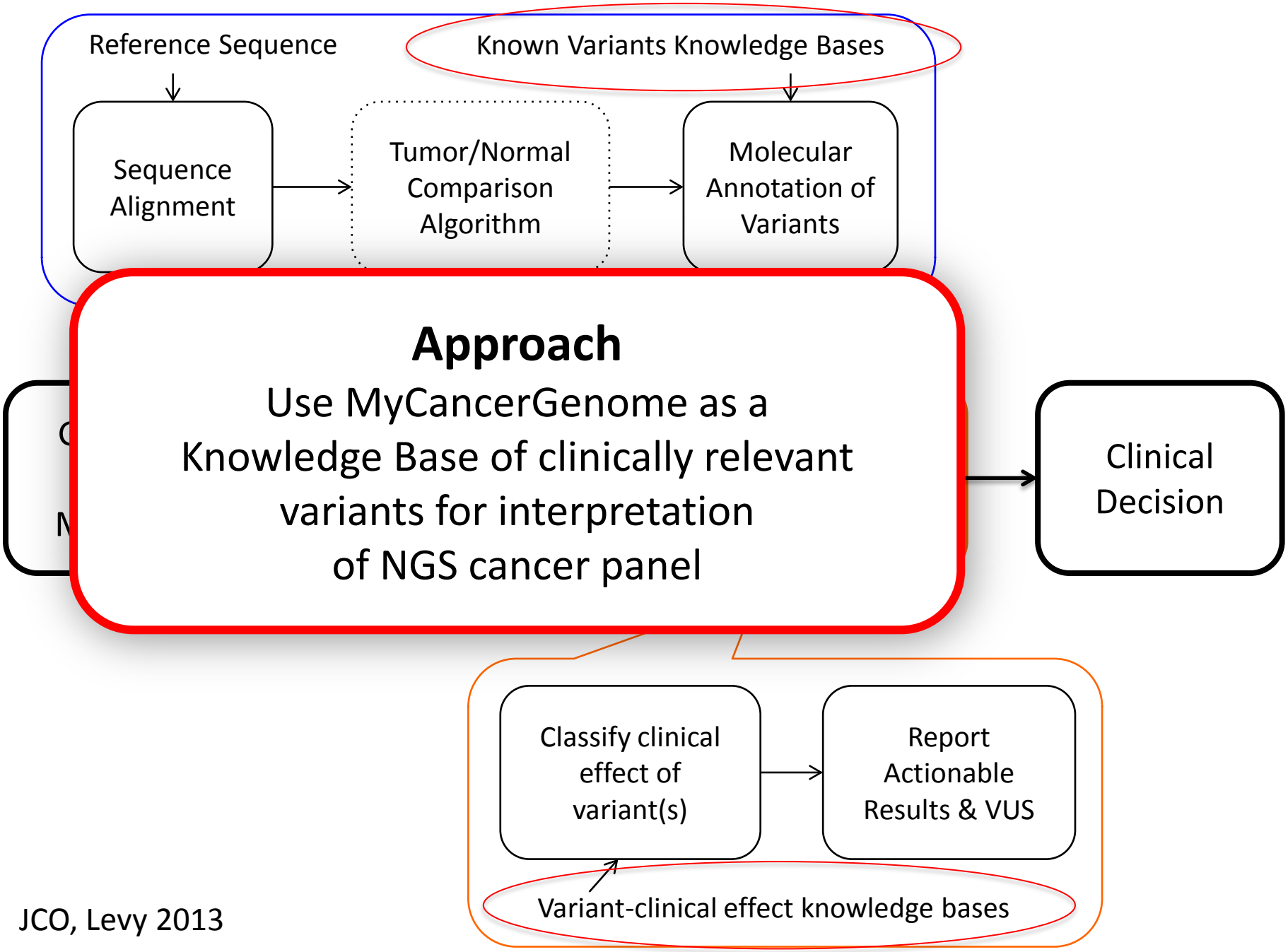
In summary, the results of this study demonstrate that this patient does have an exon 19 deletion of the *EGFR* gene. The presence of this mutation indicates that this tumor will likely be responsive to EGFR inhibitors. It is importatnt to note that this assay is specific for these four mutations and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

40 Variants
6 Genes

MR#	Patient Name	Actions	Tumor Gene Mutations: H-SMP	BRAF	CTNNB1	GNA11	GNAQ	KIT	NRAS
03 81	A, B M.	Actions	■	■					
03 56	A, P	Actions	■		■				■
03 35	B, J A	Actions	■						■
01 80	B, S A	Actions							
02 29	E, J E	Actions	■					■	
02 27	F, R M	Actions							
02 77	G, T	Actions							
02 73	H, A	Actions	■			■			
03 64	S, C	Actions	A						
02 79	S, A S	Actions	R						
02 40	W, J E I	Actions							
03 74	W, C L	Actions	■	■					

1000s Variants
100s Genes

Next Generation Sequencing?



JCO, Levy 2013

Decision Support for Variant Analysis

Actionable for Tumor Type

Actionable for Other Tumor Type

Not Actionable

QC Metrics | **Actionable for Tumor Type** | Actionable Other | Non-Actionable | Clinical Trials | Patient | REPORT

Variant Info	Ref:Alt	PGM Info	PGM Alignment (Click for BAM Pileup)	PGM Call	PGM Decisio
Count: 0 Total (0 Confirmed) See More Information					
Gene: EGFR Position: 7:55249071-55249071 G Change: c.2369C>T AA Change: T790M Mutation Type: Substitution - Missense Count: 0 Total (0 Confirmed) See More Information	C:T	Total Reads: 500 Variant Reads: 401 VAF: 0.802 QUAL: 100 Q Score: (80/80)		Detected	Detected
Gene: EGFR Position: 7:55259515-55259515 G Change: c.2573T>G AA Change: L858R Mutation Type: Substitution - Missense Count: 0 Total (0 Confirmed) See More Information	T:G	Total Reads: 550 Variant Reads: 500 VAF: 0.909 QUAL: 100 Q Score: (80/80)		Detected	Detected

Decision Support for Variant Interpretation & Reporting

Patient Information

Name: Charles F Bingley
DOB: 4/12/75 **Gender:** Male **MRN:** 10101
Pathologic Diagnosis:

Specimen Information

Specimen Type: primary
Collection Date: 11/1/14
Date Received: 11/2/14

NGS RESULTS

Detected Alterations With Therapeutic Implications

Gene	Alteration	Type of Mutation
EGFR	T790M	Substitution - Missense
EGFR	L858R	Substitution - Missense

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

Approved Drugs	Variants Detected	Response to Therapy	Condition	Line of Therapy	Level of Evidence
Afatinib	EGFR L858R, EGFR T790M	Acquired resistance	Non-Small Cell Lung Cancer; When resistance mutation occurs secondary to primary sensitizing mutation in EGFR	Metastatic	NCCN
Erlotinib	EGFR L858R, EGFR T790M	Acquired resistance	Non-Small Cell Lung Cancer; When resistance mutation occurs secondary to primary sensitizing mutation in EGFR	Metastatic	NCCN
Gefitinib	EGFR L858R, EGFR T790M	Acquired resistance	Non-Small Cell Lung Cancer; When resistance mutation occurs secondary to primary sensitizing mutation in EGFR	Metastatic	NCCN

Potentially Relevant Targeted Clinical Trials - Level 3 *(see note)*

Trial Title	Conditions	Relevant Genes
Trial of Erlotinib and BKM120 in Patients With Advanced Non Small Cell Lung Cancer Previously Sensitive to Erlotinib (NCT01487265)	Non Small Cell Lung Cancer	EGFR
Phase II AZD9291 Open Label Study in NSCLC After Previous EGFR TKI Therapy in EGFR and T790M Mutation Positive Tumours (NCT02094261)	Non Small Cell Lung Cancer	EGFR
BATTLE-2 Program: A Biomarker-Integrated Targeted Therapy Study (NCT01248247)	Lung Cancer	EGFR
AZD9291 in Combination With Ascending Doses of Novel Therapeutics (NCT02143466)	Advanced Non Small Cell Lung Cancer	EGFR

Decision Support for Variant Interpretation & Reporting

Patient Information

Name: Charles F Bingley
DOB: 4/12/75 **Gender:** Male **MRN:** 10101
Pathologic Diagnosis:

Specimen Information

Specimen Type: primary
Collection Date: 11/1/14
Date Received: 11/2/14

NGS RESULTS

Detected Alterations With Therapeutic Implications *(see details in the follo*

Gene	Alteration	Type of Mutation
EGFR	T790M	Substitution - Missense
EGFR	L858R	

Variants with Potential Clinical Utility

Drug Sensitivity
In Disease (Level 1)
In Other Disease (Level 2)

Therapeutic Implications of Genomic Analysis

Approved Drugs	Variants Detected	Response to Therapy	Condition

Therapeutic Implications of Genomic Analysis, For Patient's Tumor Type - Level 1 *(see note)*

Approved Drugs	Variants Detected	Response to Therapy	Condition	Line of Therapy	Level of Evidence
Afatinib	EGFR L858R, EGFR T790M	Acquired resistance	Non-Small Cell Lung Cancer; When resistance mutation occurs secondary to primary sensitizing mutation in EGFR	Metastatic	NCCN
Erlotinib	EGFR L858R, EGFR T790M	Acquired resistance	Non-Small Cell Lung Cancer; When resistance mutation occurs secondary to primary sensitizing mutation in EGFR	Metastatic	NCCN
Gefitinib	EGFR L858R, EGFR T790M	Acquired resistance	Non-Small Cell Lung Cancer; When resistance mutation occurs secondary to primary sensitizing mutation in EGFR	Metastatic	NCCN

AZD9291 in Combination With Ascending Doses of Novel Therapeutics (NCT02143466)	Advanced Non Small Cell Lung Cancer	EGFR

Decision Support for Variant Interpretation & Reporting

Patient Information

Name: Charles F Bingley
DOB: 4/12/75 **Gender:** Male **MRN:** 10101
Pathologic Diagnosis:

Specimen Information

Specimen Type: primary
Collection Date: 11/1/14
Date Received: 11/2/14

NGS RESULTS

Detected Alterations With Therapeutic Implications *(see list following page)*

Gene	Alteration	Type of Mutation
EGFR	T790M	Substitution - Missense
EGFR	L858R	Substitution - Missense

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 *(see list)*

Approved Drugs	Variants Detected	Response to Therapy	Condition	Line of Therapy	Lev Evid
Afatinib	EGFR L858R,	Acquired	Non-Small Cell Lung Cancer; When resistance mutation occurs	Metastatic	NCCN

Potential Clinical Trials (Level 3)

Potentially Relevant Targeted Clinical Trials - Level 3 *(see note)*

Trial Title	Conditions	Relevant Genes
Trial of Erlotinib and BKM120 in Patients With Advanced Non Small Cell Lung Cancer Previously Sensitive to Erlotinib (NCT01487265)	Non Small Cell Lung Cancer	EGFR
Phase II AZD9291 Open Label Study in NSCLC After Previous EGFR TKI Therapy in EGFR and T790M Mutation Positive Tumours (NCT02094261)	Non Small Cell Lung Cancer	EGFR
BATTLE-2 Program: A Biomarker-Integrated Targeted Therapy Study (NCT01248247)	Lung Cancer	EGFR
AZD9291 in Combination With Ascending Doses of Novel Therapeutics (NCT02143466)	Advanced Non Small Cell Lung Cancer	EGFR

Detailed Summary of Alteration In Disease

Detected Alterations With Therapeutic Implications in Patient's Tumor Type - Level 1 *(see note)*

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 a

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

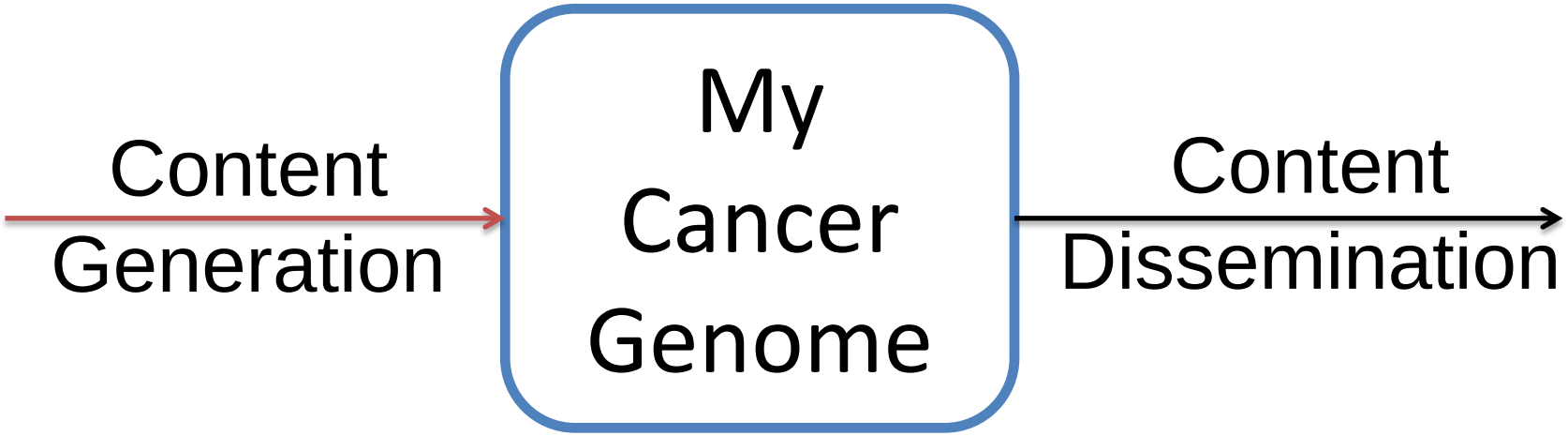
Reference

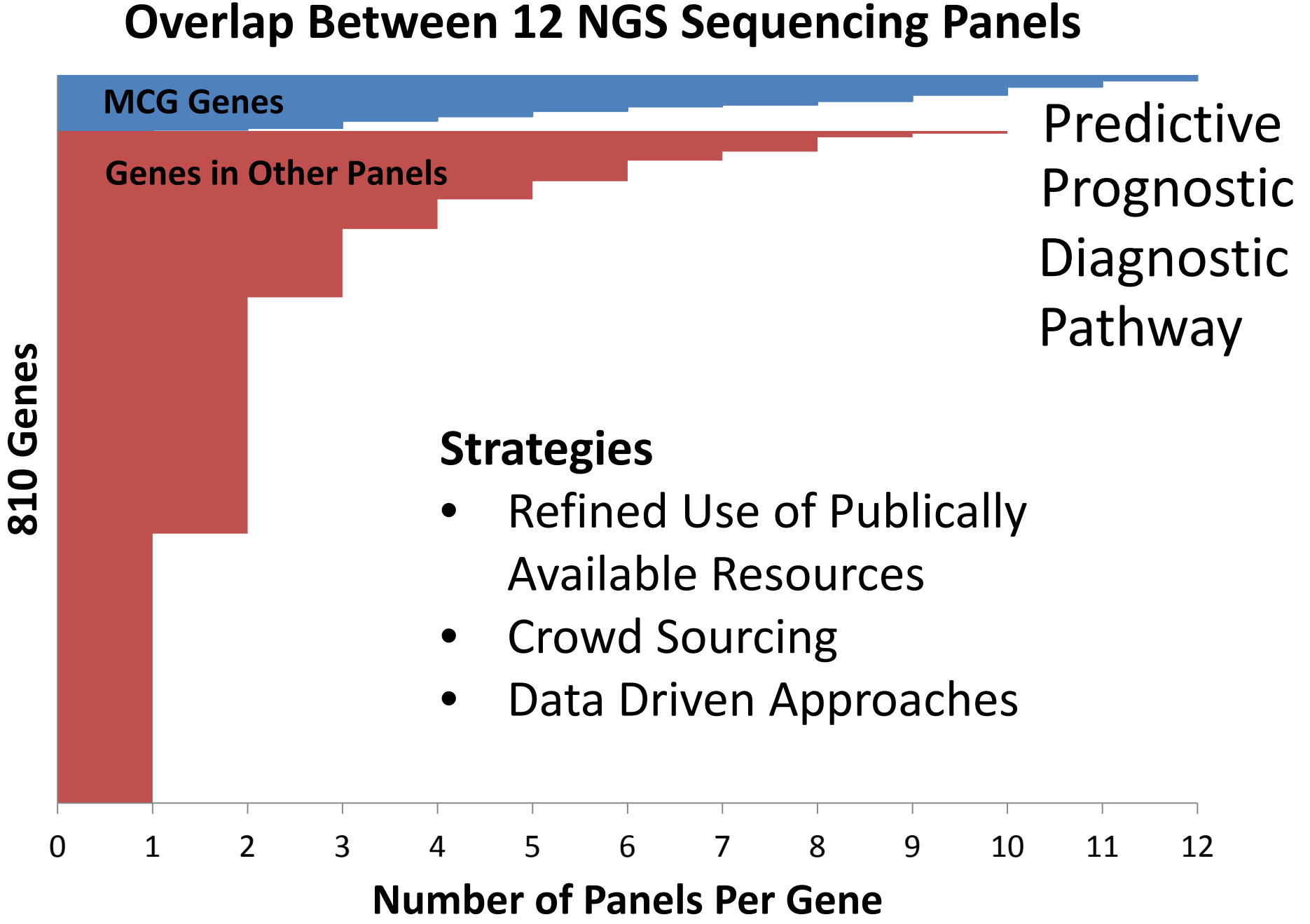
http://www.mycancergenome.org/content/disease/lung-cancer/egfr/4

Content from
My Cancer Genome

Link to
MyCancerGenome.org

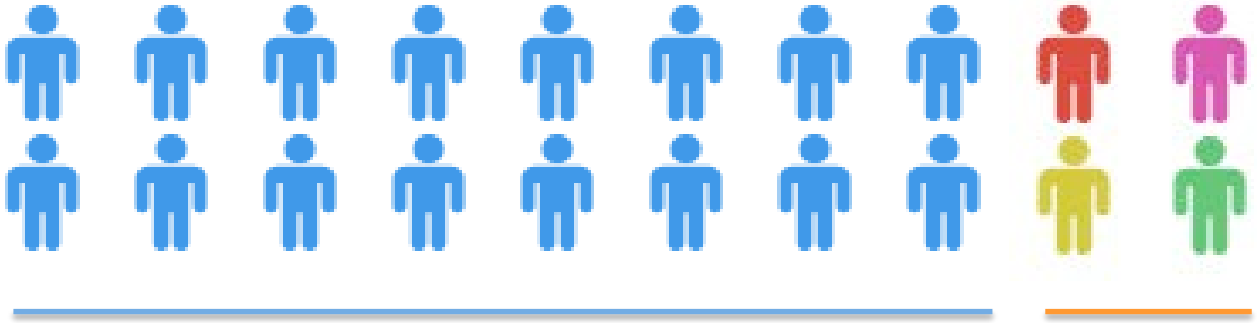
Challenges &Future Directions




Overlap Between 12 NGS Sequencing Panels
MCG Genes
Genes in Other Panels
Predictive
Prognostic
Diagnostic
Pathway
Strategies
• Refined Use of Publically Available Resources
• Crowd Sourcing
• Data Driven Approaches
810 Genes
0 1 2 3 4 5 6 7 8 9 10 11 12
Number of Panels Per Gene

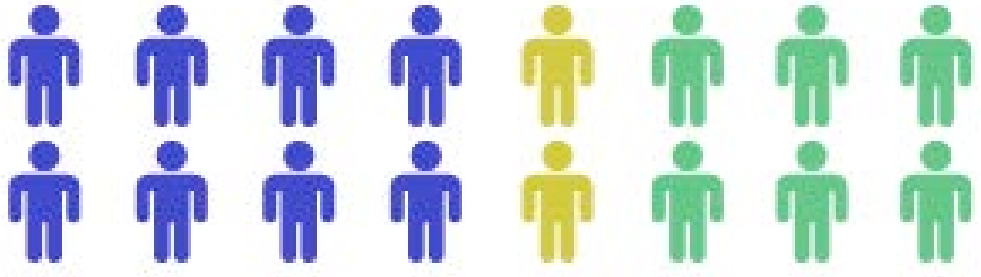
Small Sub-populations

Targeted Therapy



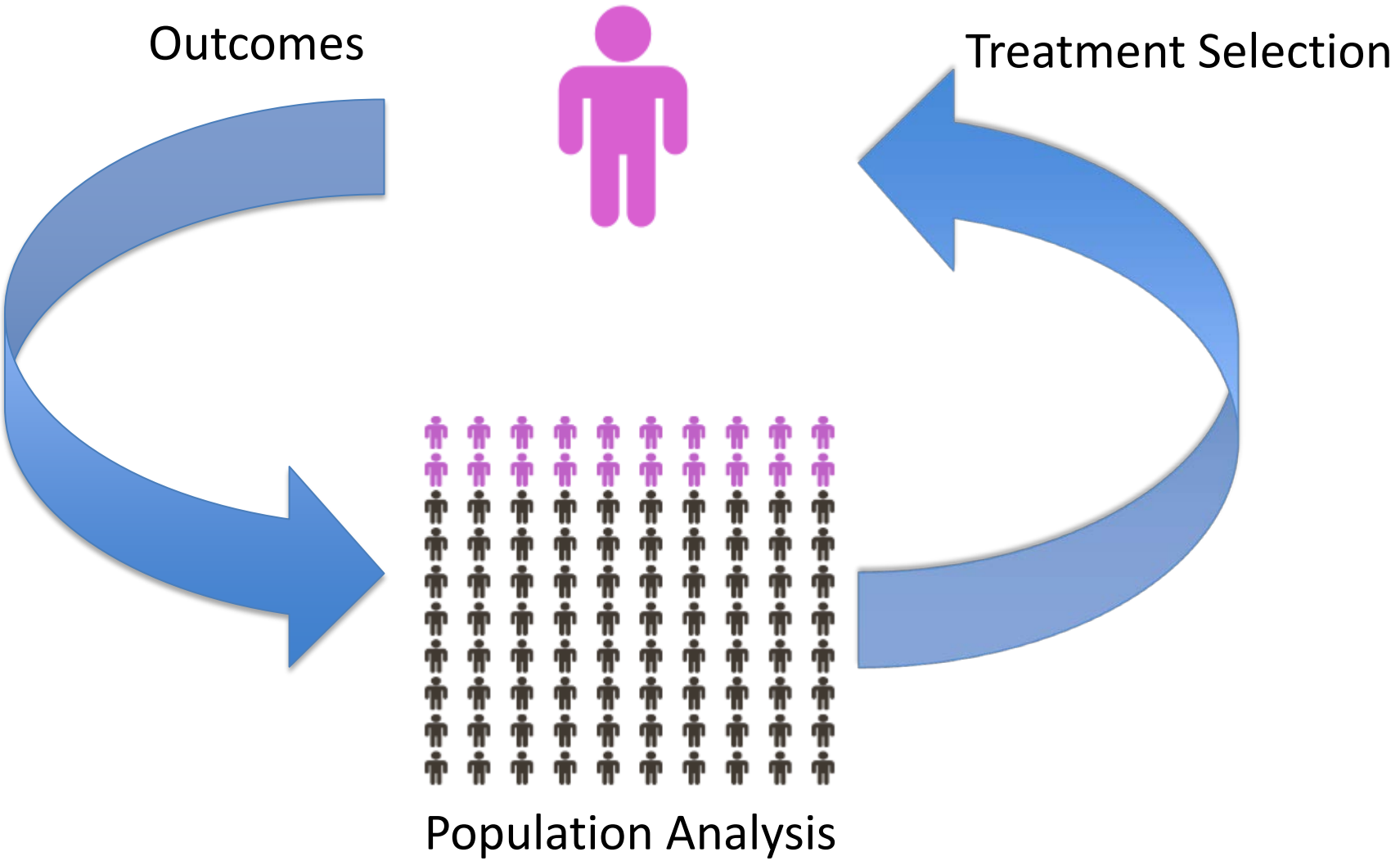
Primary Sensitivity

Primary Resistance

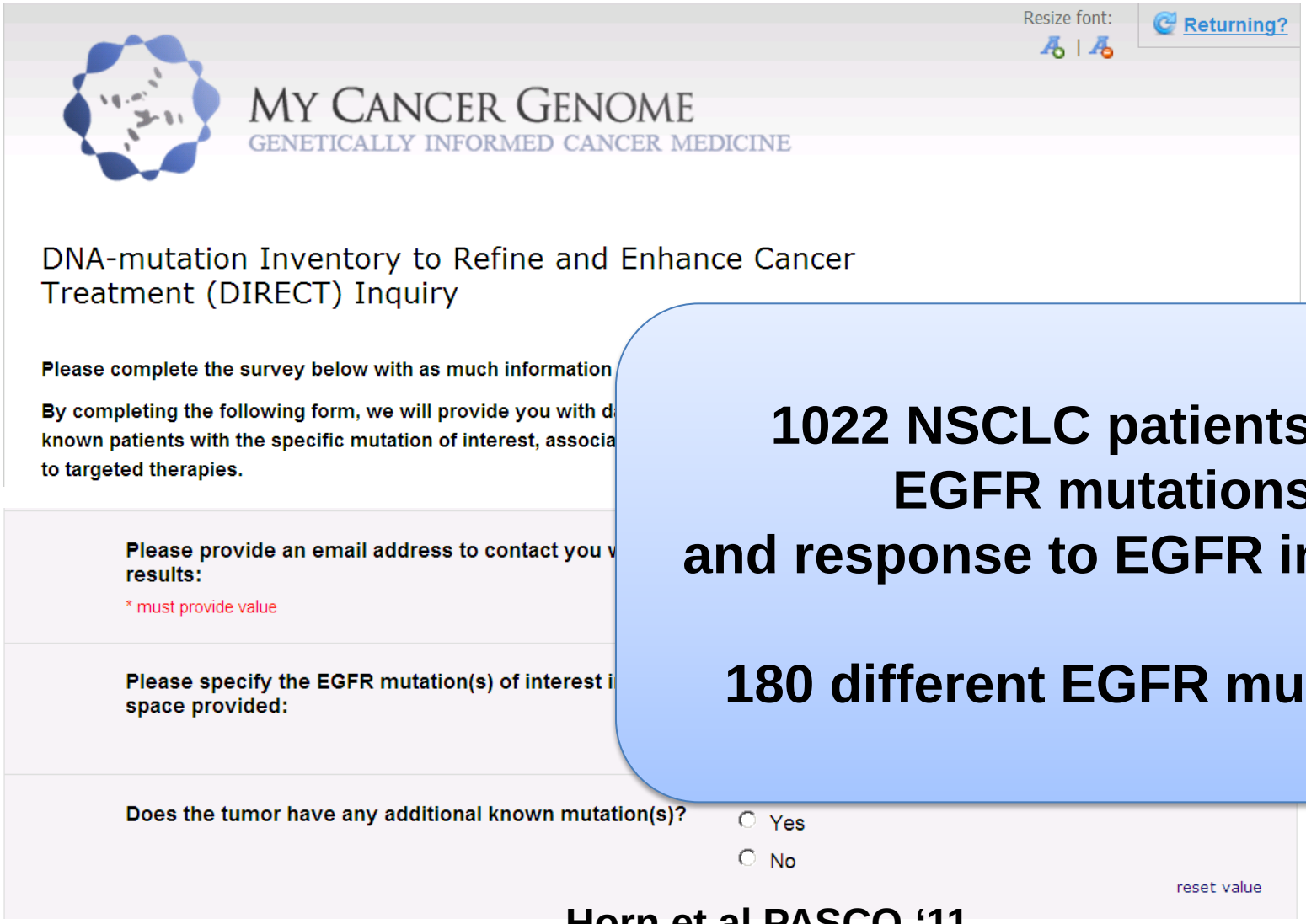


Acquired Resistance

Learning Cancer System



www.mycancergenome.org/DIRECT



1022 NSCLC patients with EGFR mutations and response to EGFR inhibitors

180 different EGFR mutations

Horn et al PASCO ‘11

Data Sharing Collaboration with Vanderbilt & Stanford
Dynamic Exploration of Melanoma Cohort

Melanoma Rapid Learning Utility

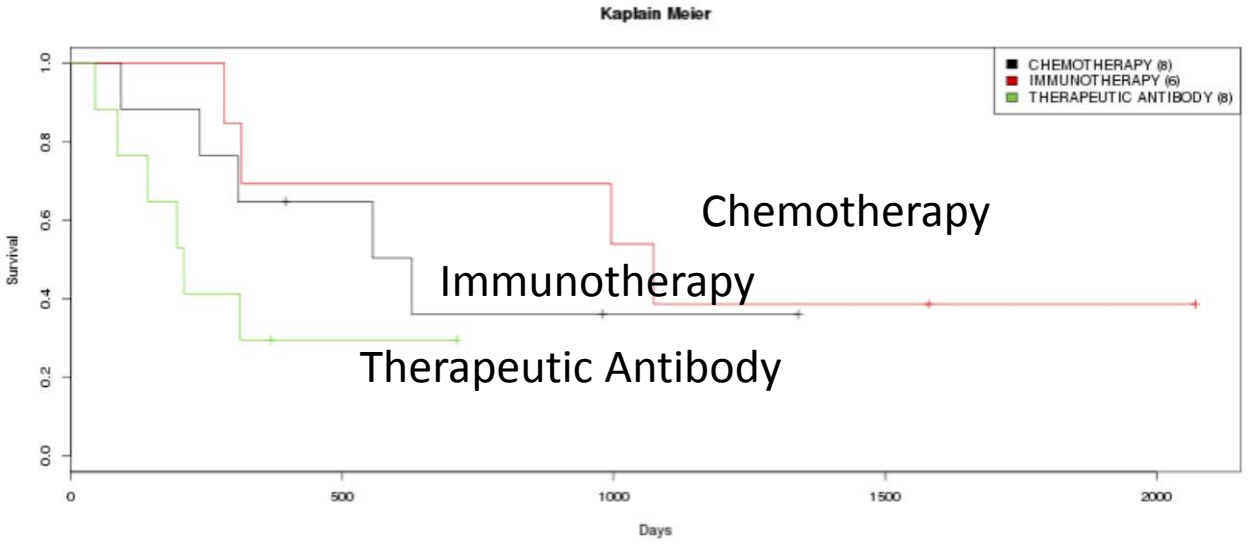
Filter by
Biomarker
Drug
Drug Class

Survival Curves

Please b
adjustme
positive r
Stratificat
Drug Cl
Outcome
Surviva
Minim
Filter By
Filter By Sex
Sex:
FEMALE
Filter By Age
Patient Age:
60
Age range
18 44.88 75.072 86
Filter By BRAF Status
Filter By NRAS Status
NRAS Test Result:
NEGATIVE
Filter By Drug Class
Compare First Two Treatments
Include:
CHEMOTHERAPY
IMMUNOTHERAPY
KINASE INHIBITOR
THERAPEUTIC ANTIBODY
Quick Check/Uncheck All Classes:
Check All
Uncheck All
Filter By Drug Name

Cohort Summary | Outcomes Analysis | Raw Data (Cohort S

Kaplan Meier | Tumor Response



R Call Used to Construct Model:

```
coxph(formula = Surv(DAYS_TO_DEATH, event = (!plot.data$R.CENSORED),
    type = "right") ~ 1 + strata(DRUG_CLASS), data = plot.data)
```

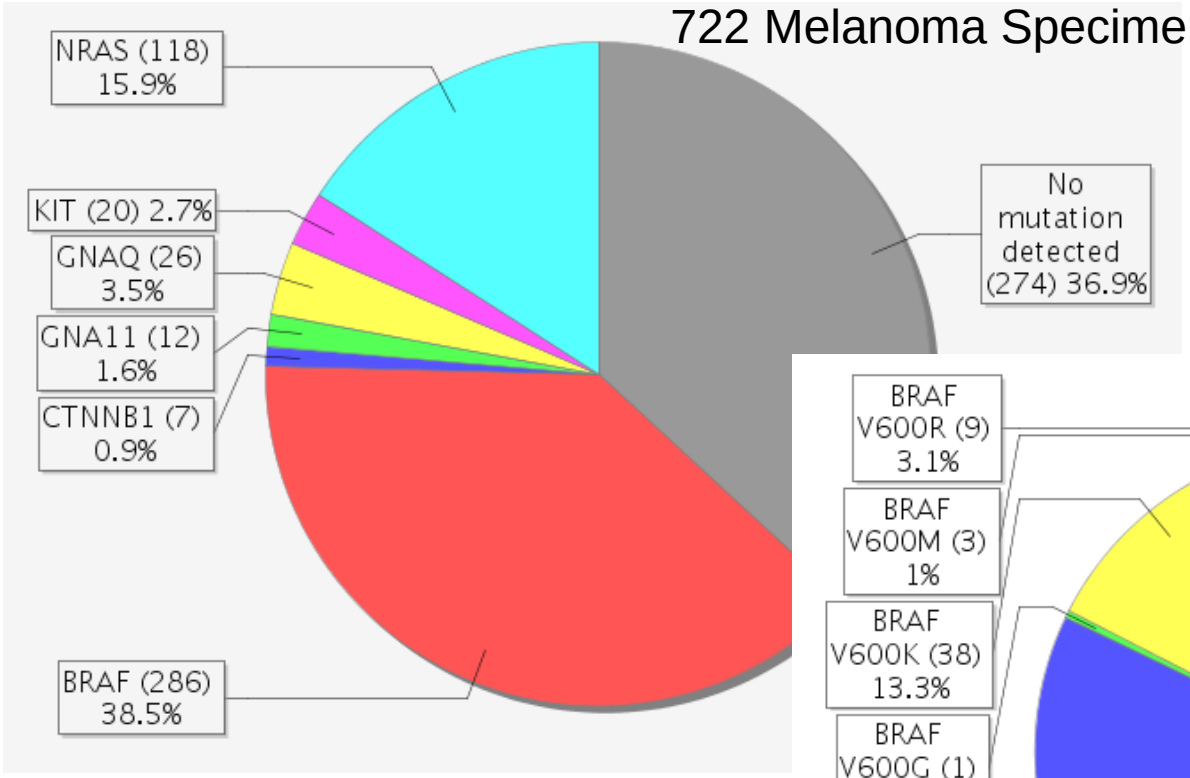
Model Summary

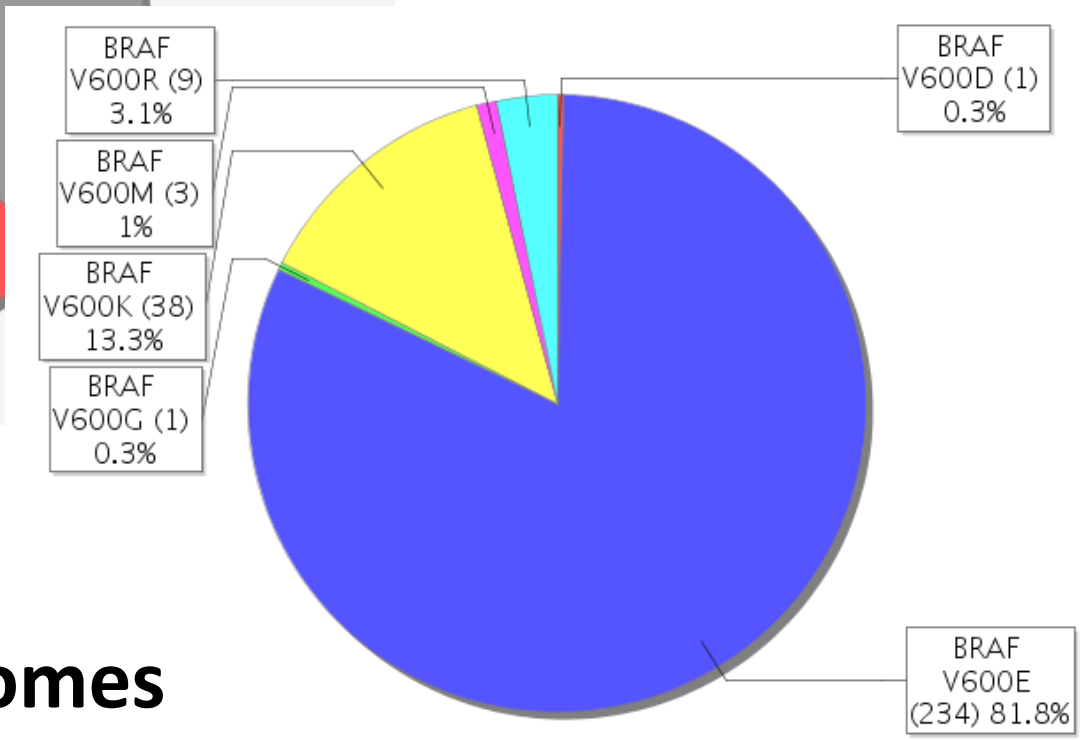
	records	n.max	n.start	events	median	0.95LCL	0.95UCL
DRUG_CLASS=CHEMOTHERAPY	8.00	8.00	8.00	5.00	628.00	308.00	
DRUG_CLASS=IMMUNOTHERAPY	6.00	6.00	6.00	4.00	1074.00	315.04	
DRUG_CLASS=THERAPEUTIC ANTIBODY	8.00	8.00	8.00	6.00	208.00	142.00	

Difference Statistics

R Call	survdiff(formula = Surv(DAYS_TO_DEATH, event = (!plot.data$R.CENSORED), type = "right") ~ DRUG_CLASS, data = plot.data)
Chi Squared Statistic	4.111486
P-Value	0.1279977

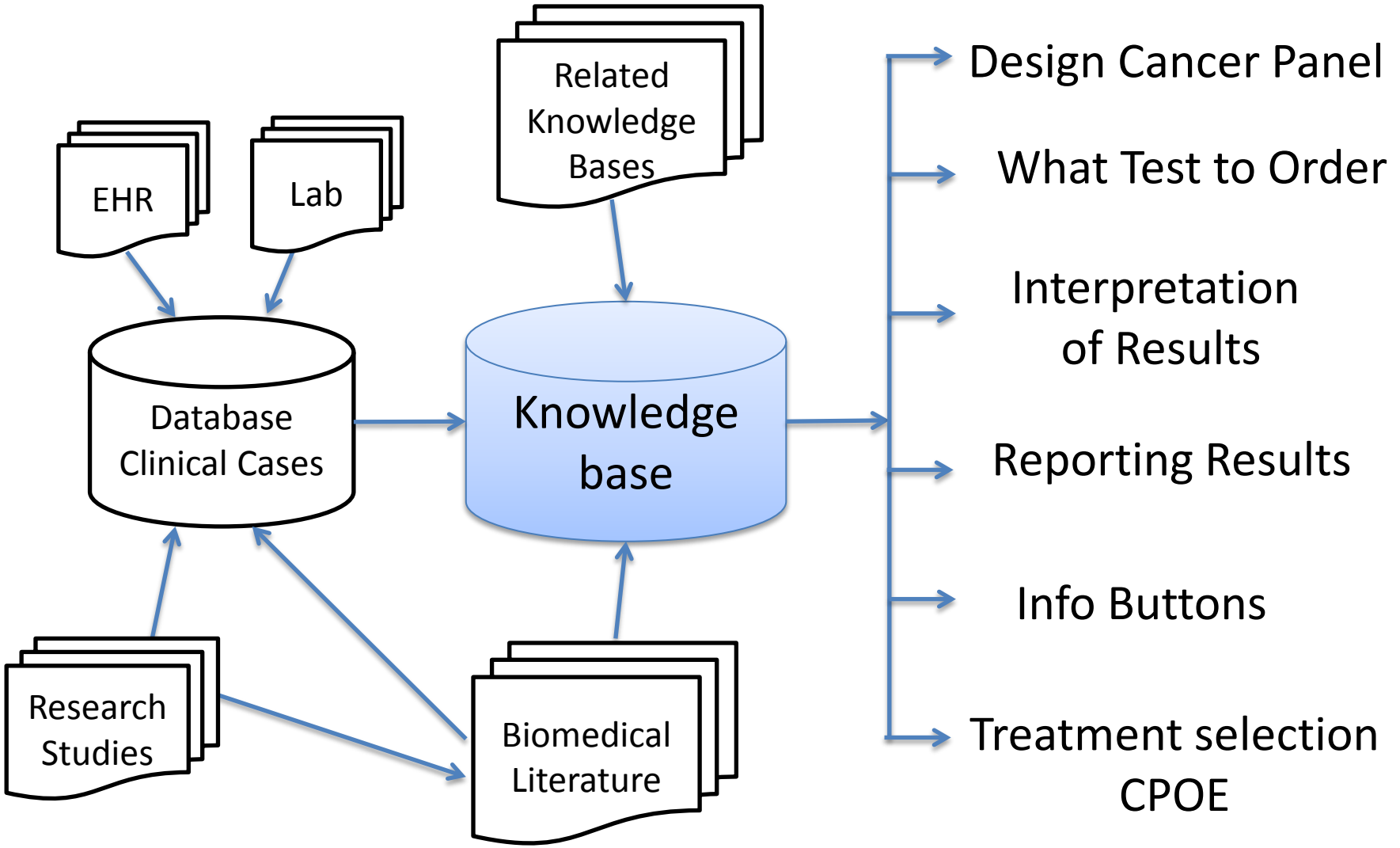
Automated Analysis Mutation Frequency





Link to Clinical Outcomes

Infrastructure for Clinical Decision Support



Health Literacy & Learning Styles

- **Patients** (*PI: Guise, co-PI:Koonce*)
  - Using health literacy and learning styles to guide oncology patients through the pharmacogenetic maze
  - Patient focused content with evaluation
  - Genetic perl videos

- **Providers** (*PI: Levy, co-PI:Kusnoor)*
  - Learning style assessment in healthcare professionals to address knowledge gaps around novel treatment strategies to overcome resistance to endocrine therapy in ER+ breast cancer
  - Develop and evaluate provider content based on learning styles

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

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- MCG Alumni
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- ONC/NCI Health 2.0 Developer Challenge
- GE Healthymagination Challenge

Industry Partner

- GenomOncology

Thank You

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