



A Teaching Affiliate
of Harvard Medical School

American Clinical Laboratory Association Results for Life Campaign

Molecular Genotyping and Targeted Therapies The Revolution in Cancer Care

Mara Bloom, JD, MS, Executive Director
Massachusetts General Hospital
November 17, 2011



MASSACHUSETTS
GENERAL HOSPITAL

CANCER CENTER

MGH Cancer Center Molecular Genotyping Program

- MGH launched first multiplex molecular genotyping test in clinical setting in fall 2009
- Assay tests 120 mutations across 16 cancer genes
- High-throughput screening of tumor samples in paraffin block – 2-3 week turnaround
- Available for most solid tumors in CLIA lab billable to payors

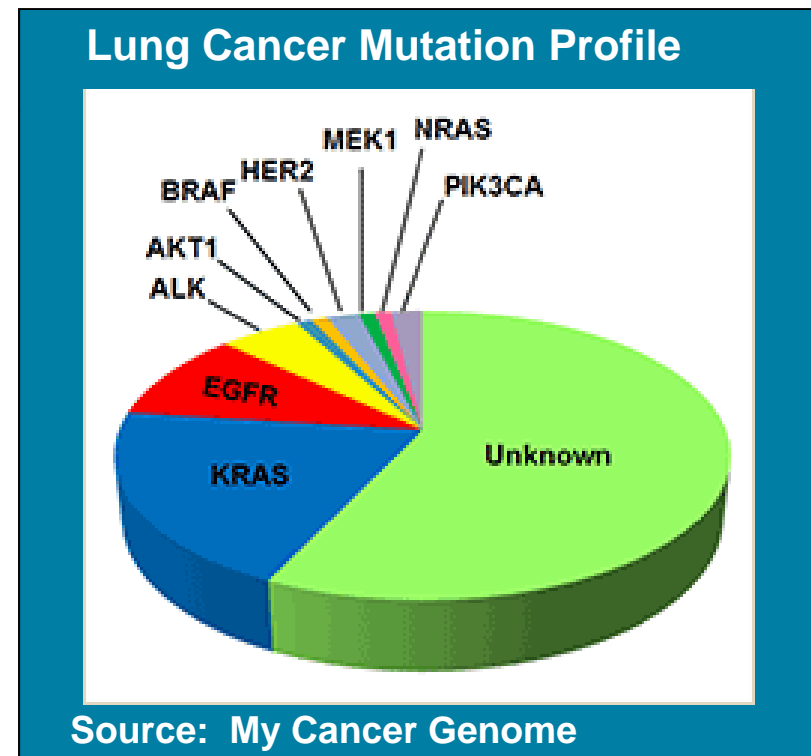


Genotyping & Targeted Therapies Program Goals

- **Better cancer diagnoses**
- **Earlier intervention -- more effective and safe therapy**
- **Better quality of life**
- **Long term cost savings**
- **Faster drug development**

Cancer Types	Pathway	Drug
Lung	EGFR	Erlotinib
Lung	ALK	Crizotinib
Melanoma	BRAF	PLX4032
Breast, Kidney, Neuroendocrine	PI3K/mTOR	Everolimus
Breast, Gastric Cancer	HER 2	Lapatinib, Pertuzumab, Trastuzumab
Breast, Sarcoma	IGF1R	Dalotuzumab

Source: MGH Cancer Center

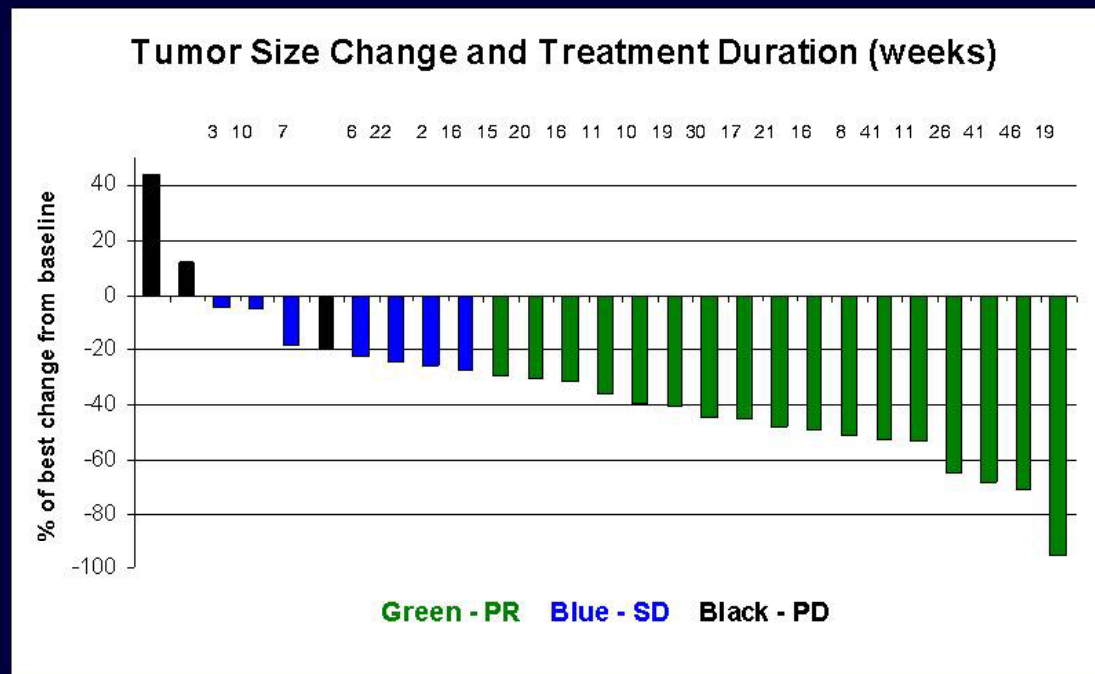


MASSACHUSETTS
GENERAL HOSPITAL

CANCER CENTER

Clinical Trials Transformation

“Waterfall Plot” of PF-02341066 Activity in NSCLC Pts. with EML4-Alk Mutation



Shaw, World Conf on Lung Cancer 2009



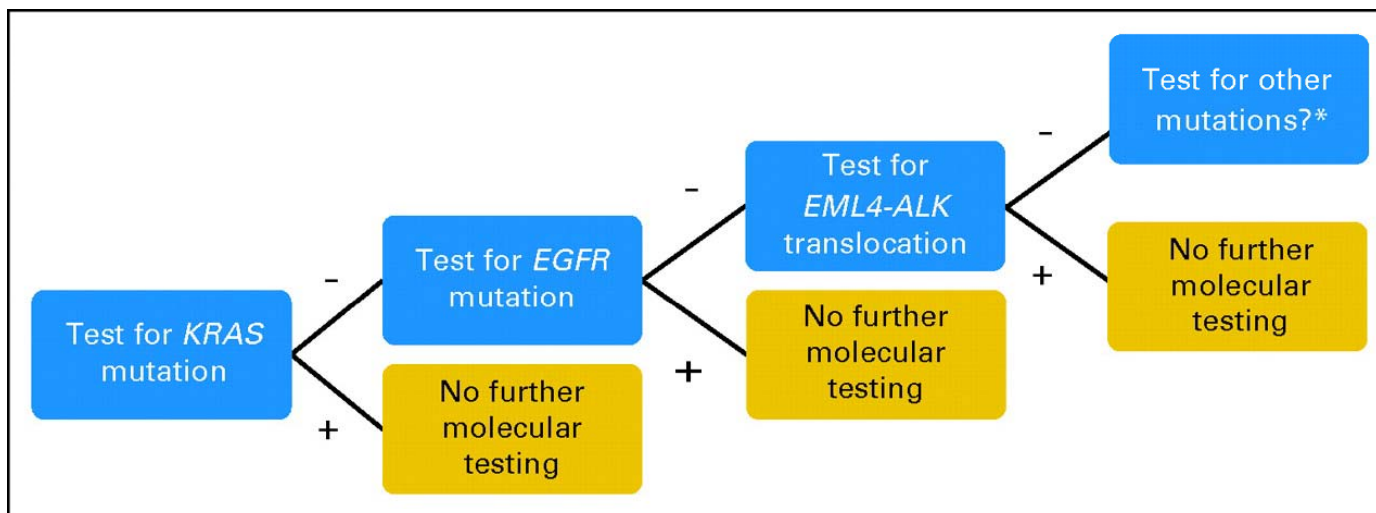
MASSACHUSETTS
GENERAL HOSPITAL

CANCER CENTER

Step Wise Approach -- Single Mutation Tests

Suggested Algorithm for Molecular Testing

Fig 2. Suggested algorithm for molecular testing for patients with non-small-cell lung cancer with tumors of adenocarcinoma histology before treatment with oral targeted therapy



Horn, L. et al. J Clin Oncol; 27:4232-4235 2009

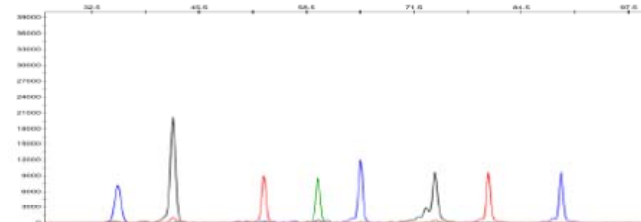


Comprehensive Approach: Multiplex Test

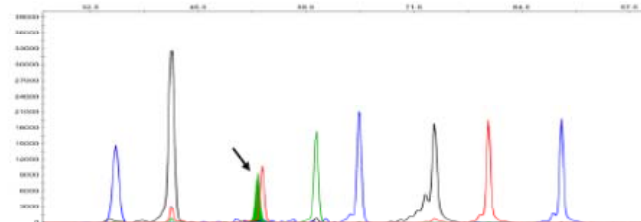
MGH Assay: 16 cancer genes – 120 mutations

Gene	Amino Acid – cDNA Residue	Gene	Amino Acid – cDNA Residue
AKT1	49G – E17	KRAS	G12 - 34G
APC	R1114 - 3340C	KRAS	G12 - 35G
APC	Q1338 - 4012C	KRAS	G13 - 37G
APC	R1450 - 4348C	KRAS	G13 - 38G
APC	T1556fs* - 4666_4667insA	NOTCH1	L1575 - 4724T
BRAF	V600 - 1798G	NOTCH1	L1801 - 4802T
BRAF	V600 - 1799T	NRAS	G12 - 34G
CTNNB1	D32 - 94G	NRAS	G12 - 35G
CTNNB1	D32 - 95A	NRAS	G13 - 37G
CTNNB1	S33 - 98C	NRAS	G13 - 38G
CTNNB1	G34 - 101G	NRAS	Q61 - 181C
CTNNB1	S37 - 109T	NRAS	Q61 - 182A
CTNNB1	S37 - 110C	NRAS	Q61 - 183A
CTNNB1	T41 - 121A	PIK3CA	R88 - 263G
CTNNB1	T41 - 122C	PIK3CA	E542 - 1624G
CTNNB1	S45 - 133T	PIK3CA	E545 - 1633G
CTNNB1	S45 - 134C	PIK3CA	Q546 - 1636C
EGFR	G719 - 2155G	PIK3CA	Q546 - 1637A
EGFR	T790 - 2389C	PIK3CA	H1047 - 3139C
EGFR	L858 - 2573T	PIK3CA	H1047 - 3140A
EGFR	E746_A750 - 2235_2240del	PIK3CA	G1049 - 3145G
EGFR	E746_A750 - 2236_2250del	PTEN	R130 - 388C
EGFR	Exon 19 deletions	PTEN	R173 - 517C
ERBB2	Exon 20 insertions	PTEN	R233 - 697C
FLT3	D835 - 2503G	PTEN	K287fs* - 800delA
IDH1	R132 - 394C	TP53	R175 - 524G
IDH1	R132 - 395G	TP53	G245 - 733G
JAK2	V617 - 1849G	TP53	R248 - 742C
KIT	D816 - 2447A	TP53	R248 - 743G
		TP53	R273 - 817C
		TP53	R273 - 818G
		TP53	R306 - 916C

Normal



Melanoma



BRAF mutation
Val600Glu
(c.1799T>A)

Source: Dora Dias-Santagata



MASSACHUSETTS
GENERAL HOSPITAL

CANCER CENTER

Genotyping Benefits vs. Single Mutation Tests

- **One test vs. multiple tests**
- **Time savings**
- **Potential cost savings**
- **Guide appropriate therapy decisions and/or clinical trials**
- **Re-contact patients as new smart drugs emerge**

Success in Targeted Therapies at MGH Cancer Center

A drug that works — for some

Researchers try to solve mystery of lung cancer medicine

By Raja Mishra



GLOBE STAFF PHOTO/S

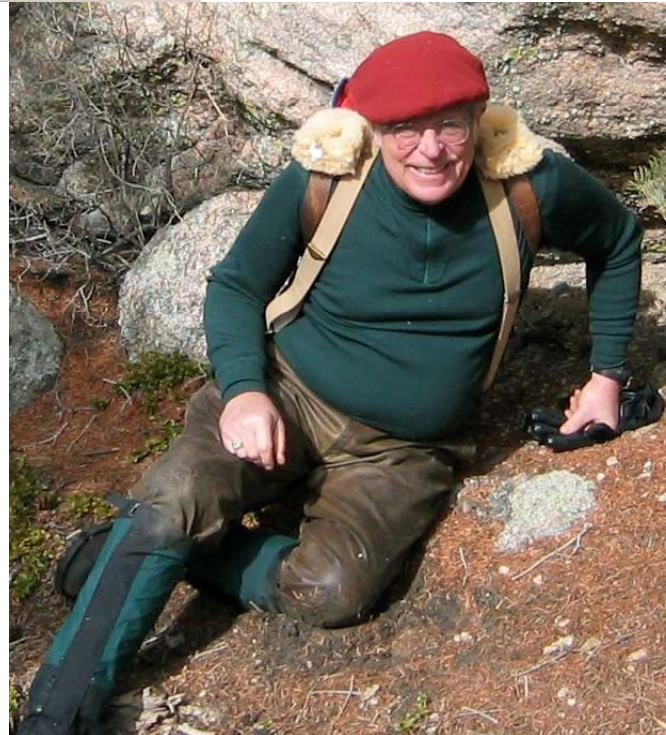
The drug Iressa has allowed Kate Robbins activities and spend precious time with her



Kate Robbins
Stage 4 Lung Cancer
Genetic abnormality: EGFR
Status: 8 year survivor



Linnea Duff
Stage 4 Lung Cancer
Genetic abnormality: EML4-ALK
Status: 5 year survivor



Greg Vrettos
Stage 4 Lung Cancer
Genetic Abnormality: EGFR
Status: 7 year survivor



John Murphy
Stage 4 Melanoma
Genetic abnormality:
BRAF and MEK
Status: 1 year survivor



MASSACHUSETTS
GENERAL HOSPITAL

CANCER CENTER

Challenges Ahead

- **Access to Genotyping**
- **Clinical Relevance**
- **Physician Education**
- **Patient Education**
- **Payor Coverage**



MASSACHUSETTS
GENERAL HOSPITAL

CANCER CENTER