My Cancer Genome™

February 2014 Volume 2, Issue 1

In This Issue

New Articles of Interest

Dai J, et al. Large-scale analysis of PDGFRA mutations in melanomas and evaluation of their sensitivity to tyrosine kinase inhibitors imatinib and crenolanib. Clin. Cancer Res. 2013 Dec 15;19(24):6935-42

Malchers F, et al. Cell-autonomous and non-cell-autonomous mechanisms of transformation by amplified FGFR1 in lung cancer. Cancer Discov 2013 Epub Dec 3

Newsletter-Related Content on MCG.org

EGFR T790M in Lung Cancer

EGFR Exon 20 Insertions in

My Cancer Genome News: Recent Grants and Awards

The Vanderbilt Knowledge Management team, working in conjunction with the My Cancer Genome team, has been awarded a two-year National Leadership Grant from the Institute of Museum and Library Services (IMLS). The purpose of the project is to define and demonstrate a scalable process for developing patient-level material about genetically informed cancer medicine. The project will develop patient-level genetic terminology in melanoma and lung cancer and will use focus groups to evaluate the terminology based on different patient learning styles.

My Cancer Genome received a one-year Charitable Giving Award from Bristol-Myers Squibb (BMS). The award will be used to support several areas of content and feature expansion for the web application, including developing immuno-oncology content.

Content Update Highlight: Exon 20 Insertion Mutations in NSCLC

My Cancer Genome Lung Cancer contributing editor Daniel B. Costa, M.D., Ph.D., M.MSc., was recently the senior author of a paper published in *Science Translational Medicine* describing a series of experiments characterizing EGFR exon 20 insertion mutations in lung cancer. While the majority of EGFR exon 20 insertion mutations confer decreased sensitivity to EGFR TKIs, the paper described a variant, EGFR A763_Y764insFQEA, that was associated with response rates and disease control in three patients in a retrospective analysis. A new variant page has been added in the EGFR in NSCLC content describing the variant EGFR A763_Y764insFQEA and implications for targeted therapeutics.

Lung Cancer

EGFR A763_Y764insFQEA in Lung Cancer

Clinical Trial Search

EGFR-Associated Clinical Trials in Lung Cancer

Newsletter Archive

Nov/Dec 2013 MCG Newsletter

Oct 2013 MCG Newsletter

Sept 2013 MCG Newsletter

August 2013 MCG Newsletter

July 2013 MCG Newsletter

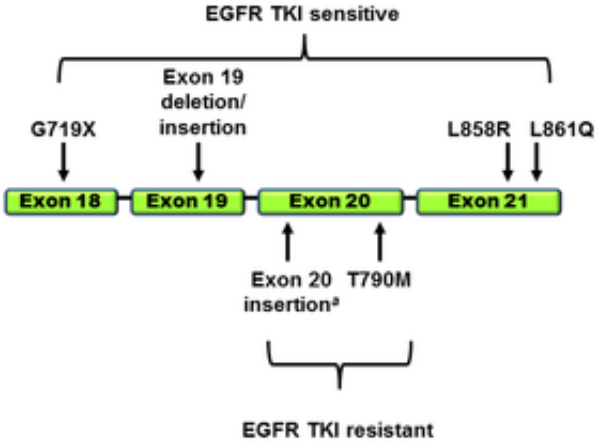
June 2013 MCG Newsletter

May 2013 MCG Newsletter

Contact Us

mycancergenome@vanderbilt.edu

www.mycancergenome.org



The figure above shows the schematic of *EGFR* mutations on the My Cancer Genome EGFR in NSCLC page. Exons 18–21 of the EGFR kinase domain are depicted. Mutations above the schematic are associated with sensitivity to EGFR TKIs. Mutations listed below the schematic are associated with EGFR TKI resistance. The figure has been updated with the "a" superscript above to indicate that while most exon 20 insertions are associated with decreased EGFR TKI sensitivity, the EGFR A763_Y764insFQEA mutation is an exception.

Content Update Highlight: Clinical Trial Table Added to EGFR c.2369C>T (T790M) Mutation in Non-Small Cell Lung Cancer Page

Advances in several mutant-selective third-generation TKIs against EGFR and a phase I trial evaluating the combination of second-generation EGFR TKIs have provided the framework for updating the EGFR c.2369C>T (T790M) Mutation in Non-Small Cell Lung Cancer page with a Clinical Trial Table for this cohort. In a phase I trial (AURA) presented at ESMO 2013, several responses were reported in patients with EGFR T790M-positive NSCLC when treated with the third-generation EGFR TKI AZD9291. In a phase I trial presented at the World Conference on Lung Cancer 2013, CO-1686 also demonstrated efficacy in this patient population. In a large phase I trial, 53 patients in a subgroup with NSCLC with the EGFR T790M mutation progressing on erlotinib or gefitinib demonstrated a 38% response rate when treated with the combination of afatinib and cetuximab. Response rates and survival endpoints from the Phase IIb/III LUX-Lung 1 study and the Phase II LUX-Lung 4 study of patients with NSCLC progressing on erlotinb or gefitinib and treated with afatinib are also included in the clinical trial table.

Reference	Study Type / Phase	Line of Treatment	Treatment Agent	Mutation Status/Group	# Patients in Study	Response Rate	PFS (months)	OS (months)
Miller et al. 2012	Phase IIb/III (LUX-Lung 1)	3rd–4th (acquired resistance to EGFR TKIs)	afatinib + best supportive care	NSCLC progressing on prior erlotinib or gefinitib	390	7%	3.3	10.8
			placebo + best supportive care	NSCLC progressing on prior erlotinib or gefinitib	195	<1%	1.1	12
Katakami et al. 2013	Phase II (LUX-Lung 4)	3rd–4th (acquired resistance to EGFR TKIs)	afatinib	NSCLC progressing on prior erlotinib or gefinitib	62	8%	4.4	19
Janjigian et al. 2011; Janjigian et al. 2012	Phase I	≥ 2nd (acquired resistance to EGFR TKIs)	afatinib / cetuximab	EGFR T790M	53	38%		
Soria et al. 2013	Phase I	≥ 2nd (prior EGFR TKI required)	CO-1686	EGFR T790M	31 (evaluable N=4)	75%		
Ranson et al. 2013	Phase I (AURA)	≥ 2nd (prior EGFR TKI required)	AZD9291	NSCLC progressing on prior EGFR TKI and T790M expansion cohort	27	2 confirmed PRs reported in T790M mutation positive patients		

NOTE: OS = overall survival; PFS = progression-free survival; PR = partial response.

Article of Interest Highlight

First-line gefitinib in Caucasian EGFR mutation-positive NSCLC patients: a phase-IV, open-label, single-arm study

Authors: Douillard JY, Ostoros G, Cobo M, Ciuleanu T, McCormack R, Webster A, Milenkova T

Study Type: Phase IV, open-label, follow-up (to IRESSA and IPASS) study in 13 European countries. Objectives included efficacy, safety, tolerability, and comparison of baseline tumor and plasma EGFR status.

Eligibility: First-line Caucasian patients with locally advanced or metastatic NSCLC harboring an activating EGFR mutation.

Screening and Enrollment period: September 2010 to February 2012.

Study Treatment: Single-agent gefitinib taken orally 250 mg/day until disease progression or intolerable toxicity.

Results: 1060 patients were screened to enroll 118 patients with NSCLC harboring activating EGFR mutations. Overall response rate = 69.8% and median progression-free survival = 9.7 months. Median overall survival = 19.2 months. Results were consistent with phase III studies of gefitinib.

Biomarkers: Baseline tumor and plasma EGFR mutation status were compared in 652 patients with matched samples. Compared with tumor EGFR mutation status, plasma mutation status demostrated a concordance rate of 94.3%, a sensitivity rate of 65.7%, a specificity rate of 99.8%, a positive predictive value of 98.6% and a negative predictive value of 93.8%.

ENOME

Subscribe to our email list

2220 Pierce Avenue 691 Preston Research Building | Nashville, TN 37232 US