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Imielinski M. et al. Oncogenic and sorafenib-sensitive ARAF mutations in lung adenocarcinoma. *J. Clin. Invest.* 2014 Epub Feb 24

Yu HA. et al. Poor response to erlotinib in patients with tumors containing baseline EGFR T790M mutations found by routine clinical molecular testing. *Ann. Oncol.* 2014 Feb; 25(2): 423-8

Newsletter-Related Content on MCG.org

NRAS in Thyroid Cancer

Molecular Profiling of Melanoma

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

My Cancer Genome News: Leadership Update

We are happy to announce that Dr. Christine Lovly, previously deputy editor of My Cancer Genome, will become the new co-editor-in-chief. Dr. Lovly received a B.A. in chemistry from Johns Hopkins University followed by M.D. and Ph.D. degrees as part of the Medical Scientist Training Program at Washington University in St. Louis, MO. She started on faculty at Vanderbilt in the Department of Medicine, Division of Hematology-Oncology, and in Cancer Biology, in July 2012 after completing her internal medicine residency and medical oncology subspecialty training at Vanderbilt. Dr. Lovly has been involved with the planning, design, and content of MyCancerGenome.org since its inception in 2011. She is the section editor of the lung cancer, melanoma, and molecular medicine sections, as well as a contributor to the inflammatory myofibroblastic tumor (IMT) section. Dr. Lovly recently received the Damon Runyon Clinical Investigator Award for her work developing novel treatment strategies for ALK-positive lung cancer.



Co-founder and co-editor-in-chief Dr. William Pao has accepted the position of Global Head of the Oncology Disease and Translational Area in the Oncology Division of Pharmaceutical Research and Early Development at Roche in Basel, Switzerland, effective May 1st. Dr. Pao will maintain an academic affiliation with Vanderbilt's Division of Hematology/Oncology in the Department of Medicine and the Vanderbilt-Ingram Cancer Center but will have to step down from his duties at My Cancer Genome.

Dr. Mia Levy will continue in her role as co-editor-in-chief, and My Cancer Genome will maintain its focus on developing new content and features by working with contributors, collaborators, and developing partnerships. My Cancer Genome's mission will continue to be serving cancer patients by enabling them, their doctors, and cancer researchers to quickly access up-to-date information about treatments and clinical trials available to patients based on their tumor genetic profiles.

Content Update Highlight: Thyroid cancer

Clinical Trial Search

BRAF-Associated Thyroid Cancer Clinical Trials

Newsletter Archive

- March 2014 MCG Newsletter
- Feb 2014 MCG Newsletter
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Thyroid cancer rates are increasing in the United States, in contrast with decreasing or unchanging trends for many other cancer types. Recently, [KRAS](#), [NRAS](#), and [HRAS](#) content was added to the [thyroid cancer](#) section based on a [study](#) from contributor [Dr. James Fagin's](#) group. Twenty metastatic thyroid carcinoma patients refractory to radioiodine were evaluable for the study after thyrotropin alfa injections and PET-CT to determine tumor uptake levels. The MEK inhibitor selumetinib was administered at 75mg twice a day for four weeks, after which a second set of thyrotropin alfa injections and PET-CT were performed to measure post-selumetinib increases in iodine uptake. Out of the 12 of 20 patients that met a specified threshold of iodine uptake, 8 patients received therapeutic doses of iodine-131, with selumetinib dosing continuing for two days after radioiodine treatment. Of these 8 patients, one patient's tumor had a BRAF mutation, 5 patients' tumors harbored NRAS mutations, and one patient's tumor had a RET/PTC mutation. Scans were performed two and six months after radioiodine treatment. Four of the five patients with NRAS-mutant tumors experienced a partial response, and the final patient with NRAS-mutant thyroid cancer demonstrated stable disease per RECIST criteria.

The [KRAS](#), [NRAS](#), and [HRAS](#) pages in [thyroid cancer](#) have also been updated with a clinical trial summary based on two phase II trials of sorafenib in thyroid cancer patients.

Reference	Study Type / Phase	Line of Treatment	Treatment Agent	Mutation Status	# Patients in Study	Response Rate	PFS (months)	OS (months unless otherwise indicated)
Kloos et al 2009	Phase II	1st line or greater	Sorafenib	14 BRAF V600E 3 K601E	33 PTC (of these, 28 were included in the response assessments) without previous chemotherapy	15%	15	23 (Kaplan-Meier estimate of median OS)
					8 PTC with previous chemotherapy	13%	10 (Kaplan-Meier estimate of median PFS)	37.5 (Kaplan-Meier estimate of median OS)
				BRAF, HRAS, and NRAS wild type	11 HTC or FTC	0%	4.5 (Kaplan-Meier estimate of median PFS)	24.2 (Kaplan-Meier estimate of median OS)
				4 ATC	0%			
Hofman et al 2009	Phase II	1st line or greater	Sorafenib	9 BRAF V600E 1 BRAF V600E + PIK3CA mutation 2 NRAS mutations 1 KRAS mutation	32 DTC	25%	13.3	

NOTES: ATC = anaplastic thyroid cancer, DTC = differentiated thyroid cancer, FTC = follicular thyroid cancer, OS = overall survival, PFS = progression-free survival, PTC = papillary thyroid cancer.

The American Cancer Society (ACS)'s annual report on cancer statistics is published in January/February each year and includes data on incidence and death rates for many different cancer sites. The National Cancer Institute, the Centers for Disease Control and Prevention, and the North American Association of Central Cancer registries collect incidence data, while the mortality data is collected by the National Center for Health Statistics. Some cancers, such as basal cell or squamous cell skin cancers, are not reported to cancer registries and incidence and mortality data are reported elsewhere.

The incidence and mortality data for the [molecular profiling page](#) of twelve major cancer types on My Cancer Genome have been updated from the annual report from the American Cancer Society. For additional information and statistics see [ACS 2014](#) and [Siegel et al. 2014](#).

Article of Interest Highlight

[Poor response to erlotinib in patients with tumors containing baseline EGFR T790M mutations found by routine clinical molecular testing](#)

Authors: Yu H, Arcila M, Hellmann M, Kris M, Ladanyi M, Riely G

Study Type: Retrospective EMR/chart review of 2,774 patients to identify the frequency and outcomes of patients with lung cancer harboring baseline EGFR T790M

Eligibility: Patient cases with lung cancer harboring EGFR T790M in pre-treatment tumor specimens were eligible. EGFR T790M mutations could be identified via standard sequencing (4 patients), locked nucleic acid-based PCR sequencing (3 patients), and mass spectrometry-based mutation profiling assay (13 patients). Patient cases were excluded with acquired EGFR T790M after treatment with EGFR TKI.

Frequency Estimate: Patient cases at MSKCC between January 2009 through April 2013 with [ICD-O](#) codes that indicated a diagnosis of lung cancer and who had had a mass spectrometry-based mutation profiling assay performed were identified to determine the frequency of baseline EGFR T790M mutations.

Outcome Measures: Progression-free survival and overall survival (based on RECIST 1.1). Average imaging frequency was 2-3 months.

Results: In the dataset of lung cancer patients with EGFR mutations identified via mass spectrometry-based assay, the rate of baseline EGFR T790M mutations was 0.5% (11 out of 2774 patient cases). Across results from three different molecular techniques with different levels of sensitivity, 2% of pre-treatment EGFR lung cancers harbored an EGFR T790M mutation. Response rate, progression-free survival and overall survival were reported to be 8%, 2 months, and 16 months respectively, for 13 patient cases with lung cancer with baseline EGFR T790M mutations treated with erlotinib.

Related Papers:

A subset of the patient cases assessed in this study were described in a

previous paper entitled [Screening for germline EGFR T790M mutations through lung cancer genotyping](#).

Also see [Hereditary lung cancer syndrome targets never smokers with germline EGFR gene T790M mutations](#) and [Germline EGFR T790M mutation found in multiple members of a familial cohort](#).

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