MY CANCER GENOME

August 2013 Volume 1, Issue 4

In This Issue

New Articles of Interest

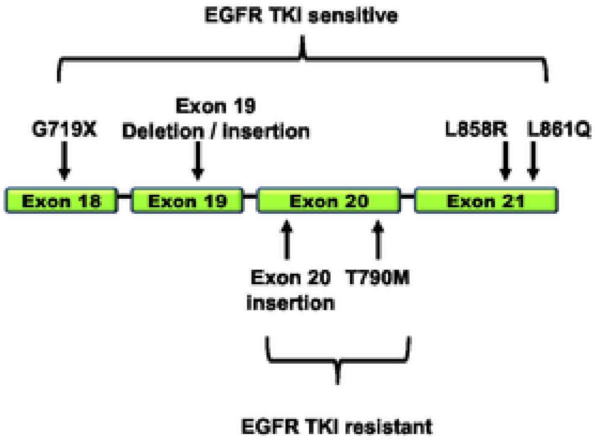
Jedd D. Wolchok, et al. Nivolumab plus ipilimumab in advanced melanoma. N Engl J Med. 2013 Jul 11;369(2):122-33.

Solange Peters, et al. Dramatic response induced by vemurafenib in a BRAF V600E-mutated lung adenocarcinoma. J Clin Oncol. 2013 Jul 10;31(20):e341-4.

Javier Munoz, et al. Rapid response to vemurafenib in a heavily pretreated patient with hairy cell leukemia and a BRAF mutation. J Clin Oncol. 2013 Jul 10;31(20):e351-2.

Philippe Bahadoran, et al. Major

My Cancer Genome Feature: The DIRECT database



My Cancer Genome houses the DNA-mutation Inventory to Refine and Enhance Cancer Treatment (DIRECT), a database of *EGFR* mutations linked with nearly 2,000 patient outcomes in lung cancer. DIRECT contains information from published literature and data provided by clinical trial investigators. We provide an online form for clinicians, researchers, and patient/caregivers from around the world to request information; My Cancer Genome staff provide reports in response to these requests via email. In the past three months, we have received requests from requestors in 15 countries and 13 US states (41% clinicians, 31% researchers, 28% patient/caregivers).

To compile the information in DIRECT, a retrospective PubMed medical subject heading (MeSH) search was used to identify patient-level, mutation-specific, drug response data. The database has been expanded to include individual patient-level data from large randomized controlled trials. DIRECT currently has information on 188 different primary *EGFR* mutations and 4 secondary *EGFR* mutations, and additional details are available in Yeh, et al. (2013). To query DIRECT for information about a specific *EGFR* mutation, users may fill out our online form.

Contributor Highlight: Faye M. Johnson, M.D., Ph.D.

Faye M. Johnson, M.D., Ph.D.

Director of THNMO Laboratory Program, Co-Chief Section of Head and Neck Medical Oncology, University of Texas, MD Anderson Cancer Center, Houston, Texas clinical response to a BRAF inhibitor in a patient with a BRAF L597R–mutated melanoma. J Clin Oncol. 2013 Jul 1;31(19):e324-6.

Newsletter-Related Content on MCG.org

BRAF Y472C Mutation in NSCLC

KIT Exon 9 Mutation in GIST

SMO D473H Mutation in Medulloblastoma

Clinical Trial Search

KIT-Associated Gastrointestinal Stromal Tumor Clinical Trials

---

Newsletter Archive

May 2013 MCG Newsletter

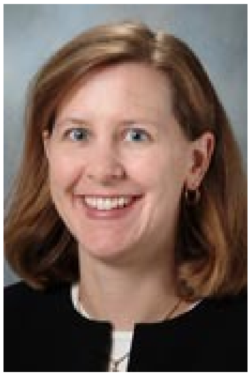
June 2013 MCG Newsletter

July 2013 MCG Newsletter

Contact Us

mycancergenome@vanderbilt.edu

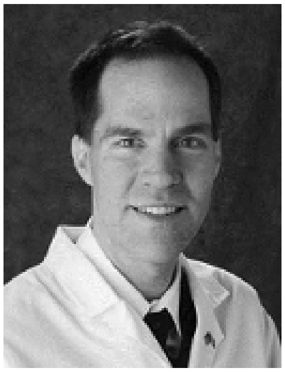
www.mycancergenome.org



Lung Cancer Contributing Editor, MyCancerGenome.org

Dr. Johnson is a contributing editor for the lung cancer section and the contributor of the NSCLC BRAF Y472C page on MyCancerGenome.org. Dr. Johnson was the senior author of a study in *Science Translational Medicine* that included an analysis of the tumor sample of an exceptional responder on dasatinib therapy with NSCLC harboring a *BRAF* Y472C kinase-inactivating mutation. This patient was previously identified in a phase II trial, in which the patient was the only one who experienced a long-duration response. Studies like this one provide the rationale for the NCI's exceptional responder initiative, to identify sub-groups of patients that respond to specific inhibitors.

Contributor Highlight: Robert G. Maki, M.D., Ph.D., FACP



Robert G. Maki, M.D., Ph.D., FACP

Professor of Medicine, Pediatrics and Orthopaedics; Director, Clinical Sarcoma Program; Steven Ravitch Chair in Pediatric Oncology, Mount Sinai Medical Center, New York, NY

GIST Section Editor, MyCancerGenome.org

Dr. Maki is a section editor for the GIST section of MyCancerGenome.org. Dr. Maki has participated in a number of studies over the past 15 years regarding the diagnosis and treatment of GIST, including co-authorship of the phase III study evaluating efficacy and safety of the multi-targeted kinase inhibitor regorafenib in GIST. A recent update of the mutational analysis comparing biomarkers in DNA and plasma samples from that trial was presented at ASCO 2013. Secondary *KIT* mutations were more commonly detected in plasma than in DNA samples, and were associated with shorter progression-free survival in those patients receiving placebo. Clinical outcomes related to *PDGFRA*, *KRAS*, and *BRAF* mutations were also reported. Dr. Maki is the recent recipient of the 2013 Sarcoma Foundation of America Nobility in Science award.

Contributor Highlight: Charles M. Rudin, M.D., Ph.D.

Charles M. Rudin, M.D., Ph.D.

Professor of Oncology, Johns Hopkins University School of Medicine, Baltimore, Maryland

Basal Cell Carcinoma and Medulloblastoma Section Editor, MyCancerGenome.org

Dr. Rudin is the section editor for the basal cell carcinoma section and the medulloblastoma section of MyCancerGenome.org, and he is the

contributor for the associated *SMO* variant pages. Dr. Rudin's lab was involved in the first clinical trials of the hedgehog signaling pathway inhibitor vismodegib in advanced tumors and in basal cell carcinoma. Recently, Dr. Rudin was the senior author of a first-in-human phase I study of the novel hedgehog inhibitor IPI-926 in advanced tumors. Dr. Rudin's lab continues to focus on preclinical investigation, early phase clinical trials and novel drug development in lung cancer and other diseases. In August, Dr. Rudin will be moving to Memorial Sloan-Kettering Cancer Center as the Chief of Thoracic Oncology.

Clinical Trial Highlight:

A Phase Ib/II, Mulicenter, Study of LEE011 in Combination With LGX818 in Adult Patients With *BRAF* Mutant Melanoma - NCT01777776

- LEE011 is an orally administered CDK4/6 kinase inhibitor
- LGX818 is an orally adminstered RAF kinase inhibitor
- This Phase Ib/II trial is investigating the combination of a CDK4/6 inhibitor with a RAF inhibitor in *BRAF* mutant melanoma patients that have received prior BRAF inhibitor therapy or are BRAF inhibitor naïve

- **Phase Ib**: 18 patients, BRAFi resistant or naïve, LGX818+LEE011
- **Phase II Arm 1a**: 60 patients, BRAFi naïve, LGX818+LEE011
- **Phase II Arm 1b**: 30 patients, BRAFi naïve, single-agent LGX818
- **Phase II Arm 2**: 40 patients, BRAFi resistant, LGX818+LEE011

Inclusion Criteria:

- Locally advanced or metastatic BRAF V600 mutated melanoma
- ECOG performance status of 0 - 2
- **Phase Ib**: Evaluable and/or measurable disease by RECIST v1.1.
- **Phase II (BRAFi naïve or resistant)**: Measurable disease by RECIST v1.1.
- Archival tumor tissue must be obtained for patients enrolled in **Phase Ib and Phase II Arm 1a/b- BRAFi naïve patients**. If an archival tumor tissue is not available, a fresh tumor sample is acceptable
- **Phase II Arm 2**, patients must agree to undergo a fresh tumor biopsy unless one was collected prior to study entry but at the time of disease relapse from the most recent BRAFi treatment

Exclusion Criteria:

- In the **phase II BRAFi naïve arms (1a/b)**, prior exposure to CDK4/6 inhibitor (e.g., PD 0332991)