MY CANCER GENOME™

November / December 2013 Volume 1, Issue 7

In This Issue

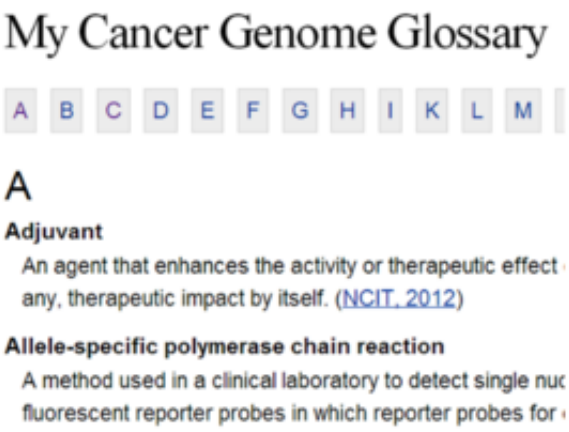
New Articles of Interest

Lim SH, Lee J-Y, Sun J-M, Kim K-M, Ahn JS, Ahn M-J, Park K. A new KIT gene mutation in thymic cancer and a promising response to imatinib. J. Thor. Oncol. 2013 Oct;8(10):e91-e92

Elisei R, Schlumberger MJ, Müller SP, Schöffski P, Brose MS, Shah MH, Licitra L, Jarzab B, Medvedev V, Kreissl MC, Niederle B, Cohen EE, Wirth LJ, Ali H, Hessel C, Yaron Y, Ball D, Nelkin B, Sherman SI. Cabozantinib in progressive medullary thyroid cancer. J. Clin. Oncol. 2013 Oct 10;31(29):3639-3646

MCG Feature: Supporting Tools and Resources

My Cancer Genome provides several supporting tools and resources that are designed to help the reader learn more about My Cancer Genome and genetically informed cancer medicine. These resources are found in the About Us tab and include videos; articles, mentions and publications; a glossary; and a list of cancer resource links.


My Cancer Genome Glossary

A B C D E F G H I K L M

A

Adjuvant

An agent that enhances the activity or therapeutic effect any, therapeutic impact by itself. (NCIT, 2012)

Allele-specific polymerase chain reaction

A method used in a clinical laboratory to detect single nuc fluorescent reporter probes in which reporter probes for

Along with a demonstration of the My Cancer Genome website in the recently revised What is my Cancer Genome? video, we have a library of 15 other videos describing different aspects of My Cancer Genome or other resources available for learning about targeted therapies. For those who want to learn more about the My Cancer Genome website, our Articles and Mentions pages catalogue more than 80 articles describing or referencing My Cancer Genome, and our Publications library houses links to scientific articles, editorials, and abstracts published by the My Cancer Genome team since 2011.

The My Cancer Genome glossary was updated in October 2013, and contains definitions for 145 terms used in My Cancer Genome content. It can be accessed from any page using the bottom navigation menu and is also accessible from the Supporting Tools Menu in the About Us tab. Finally, our Cancer Resources page links to databases, advocacy groups, and government resources such as COSMIC, Stand Up to Cancer, and ClinicalTrials.gov.

We appreciate feedback submitted by visitors about our supporting tools and resources via the online user survey.

Newsletter-Related Content on MCG.org

KRAS in Colorectal Cancer

FGFR in Breast Cancer

EGFR Exon 20 Insertions in Lung Cancer

Clinical Trial Search

FLT3-Associated Adult Acute Myeloid Leukemia Clinical Trials

EGFR-Associated Clinical Trials in Lung Cancer

Newsletter Archive

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

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Contributor Highlight: Nicholas Turner, M.D., Ph.D.

Nicholas Turner, M.D., Ph.D.

Senior Lecturer, Division of Breast Cancer Research, The Institute of Cancer Research, London, England

Breast Cancer Contributing Editor, My Cancer Genome

Dr. Turner is a contributing editor for the breast cancer section of My Cancer Genome. Dr. Turner is a senior lecturer at the Institute of Cancer Research in London, and the Breast Theme lead for the Royal Marsden NIHR Biomedical Research Centre. The Turner lab research program focuses on *FGFR* as a therapeutic target in breast cancer, mechanisms of resistance to FGFR inhibitors, and consequences of *FGFR* activation. A recent publication in *Cancer Discovery* described mechanisms of resistance in *FGFR3*-mutant cancer to FGFR inhibition using RNAi screens and implicating *EGFR* activation as a resistance mechanism. Another topic of investigation is breast cancer molecular signatures from circulating DNA samples, including detection of HER2 amplification in metastatic breast cancer.

Contributor Highlight: Alberto Bardelli, Ph.D.

Alberto Bardelli, Ph.D.

Associate Professor, University of Torino, Torino, Italy

Colorectal Cancer Contributing Editor, MyCancerGenome.org

Dr. Bardelli is a contributing editor for the colorectal cancer section of My Cancer Genome. He is the director of the IFOM Genomics and Targeted Therapies program at the Institute for Cancer Research and Treatment in Italy. Dr. Bardelli is the senior author of a paper in *Nature* describing *KRAS* amplification and mutations as mechanisms of acquired resistance to EGFR inhibitors. Notably, *KRAS* mutant alleles were present in blood samples before radiographic confirmation of progressive disease in patients treated with cetuximab, supporting the potential early use of targeted agents to treat resistance. In addition, Dr. Bardelli is the first author of a recent paper in *Cancer Discovery* examining the mechanisms of acquired resistance to EGFR-inhibitors cetuximab and panitumumab in colorectal cancer patients when *KRAS* mutations were not present. Amplification of *MET* was identified as the mechanism of resistance in tumor samples and was present in circulating DNA samples 3 months after initiating anti-EGFR treatment. Anti-MET therapies may benefit this patient population in clinical studies.

Contributor Highlight: Daniel B. Costa, M.D., Ph.D., M.MSc.

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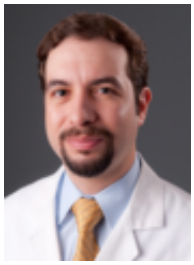

Assistant Professor, Department of Medicine, Harvard Medical School; Medical Oncologist, Hematology/Oncology, Beth Israel Deaconess Medical Center

Lung Cancer Contributing Editor, My Cancer Genome

Dr. Costa is a contributing editor for the lung cancer section and the contributor of the *EGFR* exon 20 insertion mutations in lung cancer page on My Cancer Genome. In 2012, Dr. Costa received the LCFA/IASLC Research Fellowship in Translational Lung Cancer Research for his group's research on the insensitivity of *EGFR* Exon 20 insertions to currently approved EGFR tyrosine kinase inhibitors (TKIs). The initial efforts of this work will be presented at the 15th World Conference on Lung Cancer in October 2013 and incorporated into My Cancer Genome. Dr. Costa is the senior author of both a 2012 paper describing preclinical data and clinical implications of *EGFR* exon 20 insertion mutations published in *The Lancet Oncology*, and a 2013 paper published in the *Journal of Thoracic Oncology* describing compound *EGFR* mutations and response to EGFR TKIs.

Article of Interest Highlight:

Phase I study of quizartinib administered daily to patients with relapsed or refractory acute myeloid leukemia irrespective of FMS-like tyrosine kinase 3-internal tandem duplication status

Authors: Cortes JE, Kantarjian H, Foran JM, Ghirdaladze D, Zodelava M, Borthakur G, Gammon G, Trone D, Armstrong RC, James J, Levis M

Study Type: Phase I, first-in-human, open-label, dose-escalation study in seven centers in the United States and the Republic of Georgia

Eligibility: Patients with relapsed or refractory AML or patients with newly diagnosed AML not eligible for standard induction therapy. Patients could enroll regardless of FLT3-ITD status: FLT3-ITD positive (17 patients), FLT3-ITD negative (37 patients) or FLT3-indeterminate/not determined ("ind"; 22 patients).

Enrollment and study period: January 2007 to December 2009

Study Treatment: Quizartinib is a potent and selective FLT3 kinase inhibitor. Quizartinib at 10 dose levels (12 to 450mg) on an intermittent schedule of 14 days followed by 14-day rest Q28 days; 2 dose levels (200 to 300mg) on a daily dosing schedule. Dose escalation followed 3+3 design.

Results: Dose-limiting toxicity (DLT) observed in the continuous dosing group: grade 3 QTcF prolongation. Maximum-tolerated dose (MTD): 200mg/day of continuous dosing; no MTD was reached on the intermittent schedule.

Efficacy: Patients demonstrated a 30% response rate treated with quizartinib. Subgroups: FLT3-ITD-positive patients experienced a 53% response rate; FLT3-ITD-negative patiemts experienced a 14% response rate; FLT3-ITDind patients experienced a 41% response rate. Median survival was 14 weeks.

See My Cancer Genome content for context: *FLT3* in Acute Myeloid Leukemia