Title: The Evolution to Genomic Testing and Targeted Therapy as Standard of Care for Lung Cancer

Speaker

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Bruce E. Johnson, M.D.

Bruce E. Johnson, MD is Director of the Lowe Center for Thoracic Oncology at Dana-Farber Cancer Institute and Brigham and Women's Hospital, and Professor of Medicine at Harvard Medical School. He is the leader of the Dana-Farber/Harvard Cancer Center Lung Cancer Program and the Principal Investigator of the Dana-Farber/Harvard Cancer Center Specialized Program of Research Excellence (SPORE) in Lung Cancer.

Dr. Johnson was elected to the ASCO Board of Directors and received the ASCO Cancer Foundation's Translational Research Professorship in 2008. In 2010 he received the IASLC (International Association for the Study of Lung Cancer) Scientific Award, given to an IASLC scientist for "life-time scientific contribution in thoracic malignancy research and who has also contributed to the organization's development". In 2010 he was one of the leaders of the team that was awarded the AACR (American Association for Cancer Research) Team Science Award. This "recognizes an outstanding interdisciplinary research team for its innovative and meritorious science that has advanced or likely will advance our fundamental knowledge of cancer or a team that has applied existing knowledge to advance the detection, diagnosis, prevention, or treatment of cancer".

Dr. Johnson received his MD from the University of Minnesota and did his postgraduate training at the University of Chicago and the National Cancer Institute. He came to the Lowe Center in 1998, after serving for six years as the head of the Lung Cancer Biology section of the NCI's Medicine Branch.

INTERESTS:
Non-small cell lung cancer, Small cell lung cancer, Genomic characterization, Mesothelioma

AREA OF RESEARCH:
The impact of genomic changes on the targeted treatment of thoracic malignancies:

DF/HCC Program Affiliation
Lung Cancer, Leader
Translational Pharmacology and Early Therapeutic Trials

DF/HCC Associations
Principal Investigator, Lung Cancer SPORE
Member, Center Scientific Council

SELECTED LATEST PAPERS:

1. Tumoral cavitation in patients with non-small-cell lung cancer treated with antiangiogenic therapy using bevacizumab. Nishino M, Cryer SK, Okajima Y, Sholl LM, Hatabu H, Rabin MS, Jackman DM, Johnson BE. Cancer Imaging. 2012 Jun 29;12:225-35.
2. The impact of initial gefitinib or erlotinib versus chemotherapy on central nervous system progression in advanced non-small cell lung cancer with EGFR mutations. Heon S, Yeap BY, Lindeman N, Joshi VA, Butaney M, Britt GJ, Costa DB, Rabin MS, Jackman DM, Johnson BE. Clin Cancer Res. 2012 Jun 25
3. The BATTLE trial: personalizing therapy for lung cancer. Kim ES, Herbst RS, Wistuba II, Lee JJ, Blumenschein GR Jr, Tsao A, Stewart DJ, Hicks ME, Erasmus J Jr, Gupta S, Alden CM, Liu S, Tang X, Khuri FR, Tran HT, Johnson BE, Heymach JV, Mao L, Fossella F, Kies MS, Papadimitrakopoulou V, Davis SE, Lippman SM, Hong WK. Cancer Discov. 2011 Jun;1(1):44-53.
4. Adjuvant chemotherapy for surgically resected non-small cell lung cancer. Heon S, Johnson BE. J Thorac Cardiovasc Surg. 2012 Apr 12.
5. Making personalized cancer medicine a reality: challenges and opportunities in the development of biomarkers and companion diagnostics. Parkinson DR, Johnson BE, Sledge GW. Clin Cancer Res. 2012 Feb 1;18(3):619-24.
6. CT tumor volume measurement in advanced non-small-cell lung cancer: Performance characteristics of an emerging clinical tool. Nishino M, Guo M, Jackman DM, DiPiro PJ, Yap JT, Ho TK, Hatabu H, Jänne PA, Van den Abbeele AD, Johnson BE. Acad Radiol. 2011 Jan;18(1):54-62. Epub 2010 Oct 30.
7. CT tumor volume measurement in advanced non-small-cell lung cancer: Performance characteristics of an emerging clinical tool. Nishino M, Guo M, Jackman DM, DiPiro PJ, Yap JT, Ho TK, Hatabu H, Jänne PA, Van den Abbeele AD, Johnson BE. Acad Radiol. 2011 Jan;18(1):54-62. Epub 2010 Oct 30.

IAAO2012 Title of the Talk:

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RESEARCH ABSTRACT:

The translational research on patients with adenocarcinoma of the lung here at the Dana- Farber/Harvard Cancer Center has helped identify patient subsets that respond differently to targeted agents. Women, patients with adenocarcinoma, and those who do not smoke cigarettes are more likely to have a favorable response to gefitinib and erlotinib therapy (Iressa and Tarceva) than patients with other types of lung cancer and men respectively. This prompted my laboratory to assemble tumor cell lines from women with adenocarcinoma who either did or did not smoke cigarettes to characterize their response to gefitinib. A team composed of our laboratory and the laboratory led by Dr. Sellers and Meyerson at the Dana-Farber Cancer Institute discovered that most patients who have a clinical response to gefitinib treatment have either point mutations or deletion of amino acids from the tyrosine kinase domain of the epidermal growth factor receptor. Our laboratory showed lung cancer cell lines with epidermal growth factor cell lines with these point mutations or deletions are 100 fold more sensitive to treatment gefitinib than cell lines with wild type sequence of the epidermal growth factor receptor. The lung cancer cell lines with mutations in the epidermal growth factor receptor treated with 100 nM of gefitinib have downregulation of phosphorylated epidermal growth factor receptor. This also leads to downregulation of the downstream targets including phospho-Akt and phospho-Erk1/2 kinase. Treatment of lung cancer cells with mutated epidermal growth factor receptor with 1 micromolar gefitinib leads to apoptosis while the cells with wild type epidermal growth factor receptor undergo a G1/S arrest. Future studies will study the relationship between different mutations in the epidermal growth factor receptor, their susceptibility to different epidermal growth factor receptor inhibitors, and the signaling pathways. Prospective trials will test the impact of these epidermal growth factor receptor mutations on the treatment of patients with non-small cell lung cancer. The studies will include erlotinib treatment in previously untreated elderly patients with advanced non-small cell lung cancer (older than 70) and women with adenocarcinoma who are either never smokers or former smokers. These patients will have their tumor DNA studied for the epidermal growth factor receptor sequence, and their response, response duration, subsequent response to other chemotherapy, and survival will be recorded. This will be done to determine if there is a relationship between the epidermal growth factor receptor sequence and the outcome of patients with non-small cell lung cancer after treatment with erlotinib.