Clinical trials and biostatistics workshop: introduction and overview

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This unique workshop was designed to bring together clinicians and statisticians to discuss current problems and potential solutions to issues in the design and analysis of lung cancer clinical trials and translational science. Each of the afternoon sessions pairs an oncologist with a biostatistician (some also have a formal discussant) to present a particular issue and approach. Two evening panels explore opportunities for lung cancer trials in Asia, and different models for clinical trial conduct.

Many of the current issues arise because of the development of newer, targeted therapies. The traditional phase II endpoint of tumor shrinkage may no longer be appropriate in such settings, and there may not be good historical data on newer endpoints such as disease control rate, so new phase II and phase II/III designs are needed. In addition, the degree to which therapies are targeted (and targets can be measured) has implications for the design of phase III trials.

The ability to measure thousands of gene expression levels, gene variants or gene products brings with it the challenge of sorting through these high dimensional data sets to identify which patients will benefit from particular therapies. The goal is to use genetic characteristics of the tumor and/or the host to tailor therapy.

Finally, the hope persists that the patient’s immune system can be enhanced and used to fight cancer. This field of immunotherapy also raises particular issues of clinical trial design.

Phase II Trials - endpoints, when to randomize

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The primary objective of phase II trials is to screen a new agent or regimen for efficacy and to provide estimates of its level of activity. In this workshop we will discuss commonly used endpoints such as complete plus partial response rate (overall response rate) and their corresponding analysis and interpretation. The use of multiple-stage design to minimize increase the efficiency of screening will be discussed. The importance in the design of phase II trials to minimize the chance that a truly active agent is erroneously rejected will also be discussed. There are circumstances that randomized phase II trial may be appropriate and its correct interpretation will be discussed.

Novel clinical trial design applying Bayesian adaptive randomization for targeted therapy in lung cancer - A step toward personalized medicine

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Background: With the advancement in the understanding of multiple signaling pathways associated with lung cancer, many targeted therapies have been developed. Utilization of molecularly targeted agents can inhibit these specific aberrant pathways, hence, lead to clinical efficacy. The targeted agents, however, may not work for everyone. Biomarkers expressions can be used as indicators for the aberrant signaling to identify effective targeted therapy. Our major goals are to characterize the molecular signature of individual tumors, to offer best-fit targeted therapy to patients on the trial, and to identify promising targeted agents for future development.

Methods: We have developed the “BATTLE” program, “Biomarker-integrated Approaches of Targeted Therapy of Lung Cancer Elimination,” which consists of an umbrella screening trial and 4 parallel phase II targeted therapies trials (with erlotinib, sorafenib, vandetanib, and the combination of erlotinib and bexarotene) in advanced non-small cell lung cancer patients with prior chemotherapy. All patients will have biopsy samples taken for biomarker profile assessment prior to the randomization, then they will be classified into one of the five marker groups: 1) EGFR mutation/amplification, 2) K-ras and/or B-raf mutation, 3) VEGF and/or VEGFR expression, 4) RXR and/or cyclin