WS-01  Biostatistics & Clinical Design Workshop, Sat, Sept 1, 13:00-18:00

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.

WS-02  Biostatistics & Clinical Design Workshop, Sat, Sept 1, 13:00-18:00

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.

WS-04-01  Biostatistics & Clinical Design Workshop, Sat, Sept 1, 13:00-18:00

Designs with targeted therapies
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The study of targeted therapies in oncology requires consideration of several features that are unique to this class of agents. Trials of molecularly targeted therapies need to carefully assess whether it is appropriate to restrict the study of a targeted therapy to a population with a molecular variable that may be particularly relevant to a targeted therapy, or whether it is more appropriate to open the trial to a broader population that may experience a less consistent and robust improvement in clinical endpoints. Designs of trials with targeted therapies may also need to redefine the importance of such endpoints as maximum tolerated dose versus minimal effective dose, and of objective response versus disease control/non-progression. Trials designed as a “window of opportunity” allow for the rapid testing of a targeted therapy with a biological endpoint, while other trials with this design may incorporate novel endpoints such as metabolic imaging to assess results rapidly. Examples of clinical trials with targeted therapies in lung cancer also illustrate how early use of combinations of conventional chemotherapy and targeted therapy may obfuscate the contribution of the molecular therapy or may even produce antagonistic combinations, and of how a cross-over design may introduce new challenges in the interpretation of the contribution of a novel targeted therapy. Finally, multi-targeted single agents and combinations of different targeted therapies raise additional questions in clinical trial design of how to optimize efficacy, minimize safety risks, and evaluate the clinical benefit of regimens compared with traditional standards using more conventional agents.

WS-04-02  Biostatistics & Clinical Design Workshop, Sat, Sept 1, 13:00-18:00

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