Biomarker-driven Clinical Trials

Yi-Long Wu

Abstract
Clinical trials play a crucial role in bridging preclinical drug discovery and the randomized Phase III trial. To date, many targeted therapy agents for cancer have faced disappointing results when tested in clinical trials. In order to facilitate successful and efficient transition of a compound through the drug development pipeline, it is important to incorporate scientifically and analytically validated biomarkers into rationally designed hypothesis-testing clinical trials. One of the issues faced in biomarker discovery is the availability of tissue samples for molecular analysis. In lung cancer for example, tumor tissue for molecular analysis are readily obtained through surgical resection in the early stages of the disease, but less frequently and only as small core-needle biopsies in advanced and treatment-refractory tumors. Molecular imaging of novel biomarkers or targets can add valuable spatial dimension and temporal data that could substantially improve assessments of targeted treatment efficacy. One successful example is the use of fluorodeoxyglucose and fluorothymidine positron emission tomography for the early prediction of nonprogression in advanced non-small cell lung cancer following erlotinib therapy.

The current challenges being faced in clinical trials today include the limitations of current biomarkers and imaging agent development methodologies, particularly for the molecular analysis of small tissue specimens, as well as regulatory and reimbursement policies. China, in particular faces several barriers most notably regulatory issues, human subject protection issues, intellectual property issues, a lack of funding and resources, a fragmented infrastructure, and a shortage of trained investigators.

Key Messages:

- Biomarker-driven clinical trials are important to facilitate successful transition in the drug development pipeline.
- It is essential that the new generation of clinical trials stress on the importance of biopsies to obtain relevant tumor specimens, as well as novel statistical designs, to improve treatment outcomes.

References: