Lung Cancer Workshop VI

Application of High Resolution CT Imaging Data to Lung Cancer Drug Development: Measuring Progress

May 4-5, 2009 – Bethesda, Maryland

2009 EXECUTIVE SUMMARY

Remarkable improvements in the speed and resolution of spiral CT imaging of lung cancer have provided important new opportunities to use this technology to accelerate the process of lung cancer drug development. Over the last five years, a consortium of stakeholders including academics, pharmaceutical and imaging industry investigators, federal scientists and physicians and patient advocates have participated in this forum. We have reviewed the challenges inherent with bringing the approach forward. A summary of this progress was published in the April 2009 issue of the journal *Oncology* that outlines the dimension of these activities (Mulshine, JL., Avila, R, Yankelevitz, D and Baer T. *Lung Cancer Workshop V: Use of High-Resolution CT Imaging Data in Lung Cancer Drug Development: Measuring Progress*. Oncology 23:1-5, 2009).

The challenge is moving from a traditional subjective evaluation of a two-dimensional image to a more informative, objective, and quantitative evaluation of three dimensional volume data, performed in a dynamic analysis across time points. This moves the field from describing pictures to exploiting information derived from rigorous imaging science. The quantitative imaging setting is demanding but also may carry the potential for considerable reward. This is in an area regulated by the Food and Drug Administration (FDA). For regulatory drug approval, the precision of the quantitative imaging data must be proven to be accurate, reliable and grounded in meaningful patient outcomes. As discussed in previous Workshops, this is a complex process, but progress has been occurring.

Figure 1 summarizes the impact this Workshop has had on stimulating progress with quantitative imaging in lung cancer. Several image databases have been initiated through this process, including the RIDER database by the National Cancer Institute, The Prevent Cancer Foundation-Cornell Database and the Lung Cancer Alliance Patient-donated Database (Give-A-Scan). These databases are critical not only in accelerating the development of software measurement tools but also in providing the reference material necessary to validate proposed new image quantitative approaches yet to be developed. Such research is fundamental to eventual FDA approval.

A major accomplishment of this forum is the completion of the first neoadjuvant, window-of-opportunity trial by Dr. Nasser Altorki and colleagues using the Glaxo Smith Klein drug, pazopanib. In this trial, a group of patients scheduled to undergo curative lung cancer surgery agreed to a brief (2-3 weeks) course of oral pazopanib to determine its effect on the tumor tissue recovered at the time of the

removal of the lung cancer. As Dr. Altorki presented at the American Society of Clinical Oncology annual meeting in 2008, over 80% of the cases showed some degree of volume reduction indicating a favorable response to pazopanib. This response rate was coupled with favorable modulations of the molecular targets. As outlined at Workshop VI, the leadership of GSK decided, based on the positive neoadjuvant trial result, to move this drug into evaluation in a randomized Phase II adjuvant trial for early stage lung cancer patients at high risk for relapse. The implication is that if this new adjuvant trial is positive, GSK has a pathway to drug approval that is much faster and more economical than previous approaches. In addition, a successful adjuvant trial would be a foundation for moving toward developing a chemoprevention indication for pazopanib. One of the most important goals of this workshop series is to accelerate the process of drug development for cancer prevention. The experience with pazopanib in the neoadjuvant, window-of-opportunity trial provides a pathway for realizing this goal.

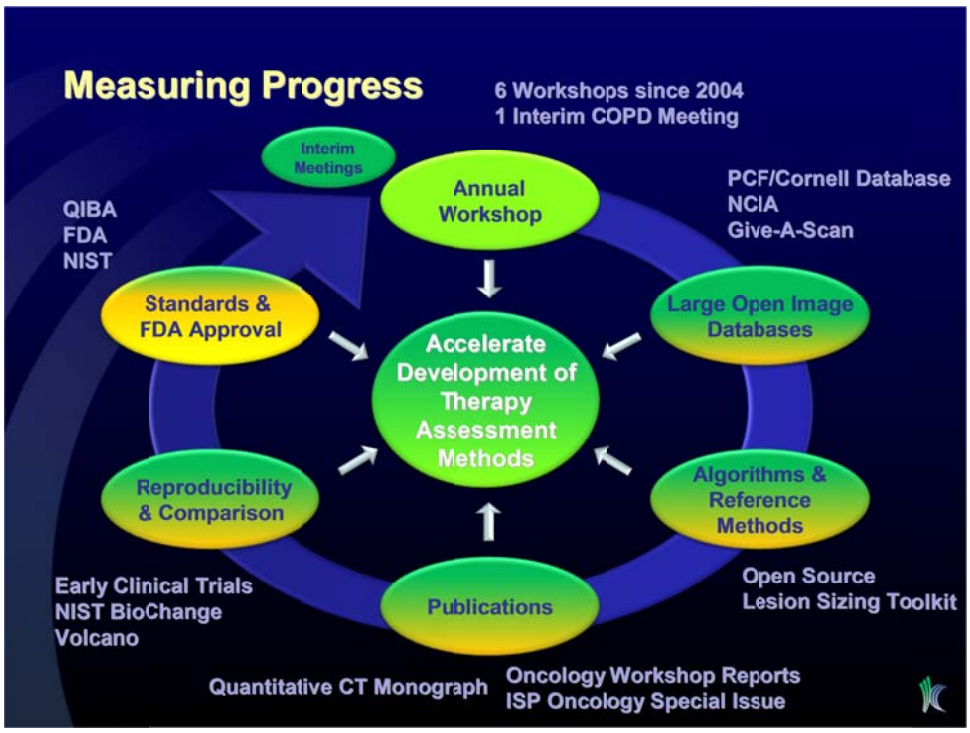

Figure 1. Workshop Accomplishments

Representatives from Roche Oncology discussed their careful plans to standardize the image acquisition protocol for a large upcoming Phase III trial in advanced stage, non small cell lung cancer. With this Abigail trial effort, Roche is also planning to make these high resolution images available for

subsequent image processing research as a contribution to further progress in this area consistent with the goals of the Workshop.

Presenters at the Workshop reviewed a number of emerging opportunities, such as with the development of several different types of imaging phantoms to be used to define issues related to image quality across different sites or different vendor platforms. The progress of the Radiological Society of North America Quantitative Imaging Biomarker Alliance (QIBA) was presented. In the Breakout Groups, an invitation was extended from an RSNA representative for the Translational Research Breakout Group to join as ad hoc members of the volume CT group of QIBA, to define an imaging protocol to be used as a standard for neoadjuvant, window-of-opportunity trials. This invitation was favorably received and the group is planning to work with RSNA in this important area as a productive collaboration.

There were presentations and detailed discussion about the progress of the Interactive Science Publishing (ISP) process of the Optical Society of America and the National Library of Medicine. The Workshop was to support this open publication tool with a dedicated supplement in the OSA journal *Optics Express* to further disseminate the tools for quantitative imaging in the drug development context.

Important updates to the Workshop from the Food and Drug Administration included extensive work in defining the magnitude of variance within and between vendor platforms as well as institutions. In addition, scientists from the National Institute of Standards and Technology and the National Cancer Institute related important progress with optimization, standardization and data collection efforts. A key innovation in this vein, presented by Kitware in collaboration with the Optical Society of America, was the introduction of an open-source, lesion sizing software toolkit. The toolkit includes an extensible lesion sizing software architecture and a set of reference methods specifically designed for CT lung lesion sizing. In addition, a turn-key lesion sizing tool based on the reference methods available in this toolkit was added to the ISP software. The software architecture, reference methods, and ISP application now provide an open framework for scientific discourse on lesion sizing algorithms and allow independent researchers to compare performance against a clear and transparent set of reference methods.

Feedback from meeting participants was overwhelmingly positive; comments were very enthusiastic and supportive. The steering committee will review all of the Workshop feedback as well as progress on the proposed upcoming activities to help plan the program for Workshop VII in 2010.