2010 Conference on Clinical Cancer Research

To address critical issues in the development of new oncology drugs, Friends of Cancer Research and The Engelberg Center for Health Care Reform at Brookings co-hosted the third-annual Conference on Clinical Cancer Research with the support of The American Association for Cancer Research (AACR), The American Society of Clinical Oncology (ASCO), and Susan G. Komen for the Cure. The conference brought together leaders in cancer drug development from federal health and regulatory agencies, academic research, and the private sector for a focused discussion on key issues surrounding the development and regulation of cancer drugs and therapies.

Dr. Varmus delivers morning keynote Dr. Hamburg delivers Afternoon Keynote
In his opening keynote address, National Cancer Institute (NCI) director, Dr. Harold Varmus, discussed the promise of targeted cancer therapies as well as the challenges inherent in developing drug combinations to target specific physiological pathways.
In her afternoon keynote address, FDA commissioner Dr. Margaret Hamburg discussed the gap between the advancement of modern science and the availability of current therapies. She stressed the need for investment in regulatory science to bridge this gap.

The following four panels presented specific topics in clinical cancer research:

Panel One – Adaptive Clinical Trials Designs for Simultaneous Testing of Matched Diagnostics and Therapeutics

- Howard I. Scher, MD, Memorial Sloan-Kettering Cancer Center
- Richard Simon, DSc, National Cancer Institute
- Rajeshwari Sridhara, PhD, US Food and Drug Administration
- Eric Rubin, MD, Merck
- Shelley Fuld Nasso, Susan G. Komen for the Cure

Panel one discussed a potential adaptive trial design that could facilitate the co-development of matched diagnostics and therapeutics. It is often not possible to identify a predictive biomarker before the start of a clinical trial to test a therapeutic. However, adaptive phase III trial designs that can identify a suitable target population during the early course of the trial would enable the efficacy of an experimental therapeutic to be evaluated within the target population as a later part of the same trial.

The use of adaptive design in phase III may offer new opportunities for matched diagnosis and treatment because the size of the trial can allow for subpopulation analysis.

The proposed design is aimed to identify a predictive biomarker and matched therapeutic in advanced prostate cancer. This included a "training set" approach in which interim analysis would be conducted on 33% of patients to identify a classifying biomarker(s). The remaining patients (the "test set") would be analyzed to determine if those positive for the predictive biomarker responded favorably to the test therapeutic. The proposed design garnered enthusiastic support and agreement that future adaptive trials for use in phase III testing could be modeled on the proposed design.

Panel Two – Identification and Elucidation of the Biology of Adverse Events: The Challenges of Safety Assessment and Translational Medicine

- Ken Turteltaub, PhD, Battelle Memorial Institute
- John Leighton, PhD, Food and Drug Administration
- Myrtle Davis, DVM, PhD, National Cancer Institute
- Leigh Ann Burns-Naas, PhD, Pfizer Inc
- Adam Clark, FasterCures

Panel two focused on how to adopt a systems biology approach to evaluating toxicities in oncology treatments and how pre-clinical safety testing currently relies heavily on outdated animal models. The panel discussed how taking advantage of emerging technologies, such as genomics and proteomics, may lead to better safety decisions based on an understanding of the biology of an adverse event.
Panelists and attendees discussed the potential for systems biology to make pre-clinical safety testing more efficient and accurate. They also voiced the hope that systems biology could eventually be used to guide the modification of a therapeutic so that desired ("on-target") effects were maintained while potential undesired ("off-target") effects were eliminated or minimized. The need for validation of systems biology approaches was also discussed as a potential concern. Panel discussion ultimately led to plans for the formation of an oncology toxicity biomarkers consortium.

Panel Three – Integrating Pain Metrics into Oncologic Clinical and Regulatory Decision-Making

- Charles Cleeland, PhD, MD Anderson Cancer Center
- Laurie Burke, RPh, MPH, Office of New Drugs, CDER, US Food and Drug Administration
- Ann O'Mara, PhD, RN, FAAN, Palliative Care Research, Community Oncology Prevention, NCI
- Martin Zagari, MD, Amgen
- Carole Baas, PhD, Advocate, Physical Sciences in Oncology, NCI

Panel three focused on how to incorporate pain metrics into clinical oncology studies and how pain measurements could contribute to regulatory decisions and/or labeling changes. Panelists looked at the prevalence and severity of cancer-related pain and that the majority of clinical trials do not include pain palliation or prevention as either a primary or secondary endpoint, due in part to the subjective nature of pain.

The panel discussed the feasibility of developing objective standards for pain measurement and that while assessments of pain would likely be in the form of patient-reported outcomes (PROs),

there is a need to develop new tools for pain measurement, such as identifying circulating biomarkers indicative of pain. The incorporation of information regarding pain palliation or prevention into labeling was also discussed. It was proposed that an accompanying trial with pain palliation as the primary endpoint could lead to pain or other symptom labeling for an NDA/BLA. It was noted that this would be in conjunction with a phase 3 trial with a more traditional primary endpoint, such as overall survival or progression-free survival.

Panel Four: Using Patient-Initiated Study Participation in the Development of Evidence for Personalized Cancer Therapy

- Stephen Friend, MD, PhD, Sage Bionetworks (Co-chair)
- Richard L. Schilsky, MD, University of Chicago (Co-chair)
- Laurie Fenton Ambrose, Lung Cancer Alliance
- Ken Buetow, PhD, National Cancer Institute
- Jamie Freedman, MD, PhD, GlaxoSmithKline
- Sue Jane Wang, PhD, US Food and Drug Administration

Panel four discussed a possible patient-initiated process for collecting patient information to potentially lead to label changes on already approved oncology drugs. Patients would contribute biological specimens in addition to detailed diagnostic, clinical, and demographic data to a common database.

Analysis of phenotypic or molecular traits could help identify patient subgroups that are unlikely to respond to specific therapeutics already on the market. Data obtained in this fashion may be used to alter the labeling to indicate a more defined subset of patients fit to receive a therapy. The panel described a potential pilot study for non-small cell lung cancer to identify molecular signatures indicative of non-response to chemotherapy. Panel discussion focused on the feasibility of engaging patients to contribute, how to minimize bias in patient accrual, and the type of data and statistical analyses that might be needed to support a post-approval labeling revision. Sage Bionetworks plans to proceed with the study, which could form a model for future patient-initiated studies.