



Oncology Biomarker Qualification Initiative: NCI-FDA-CMS Collaboration to Speed Development of Cancer Therapies

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“The emerging use of cancer biomarkers may herald an era in which physicians no longer make treatment choices that are based on population-based statistics but rather on the specific characteristics of individual patients and their tumor.”

*William S. Dalton
and Stephen H. Friend
Science; May 26, 2006*

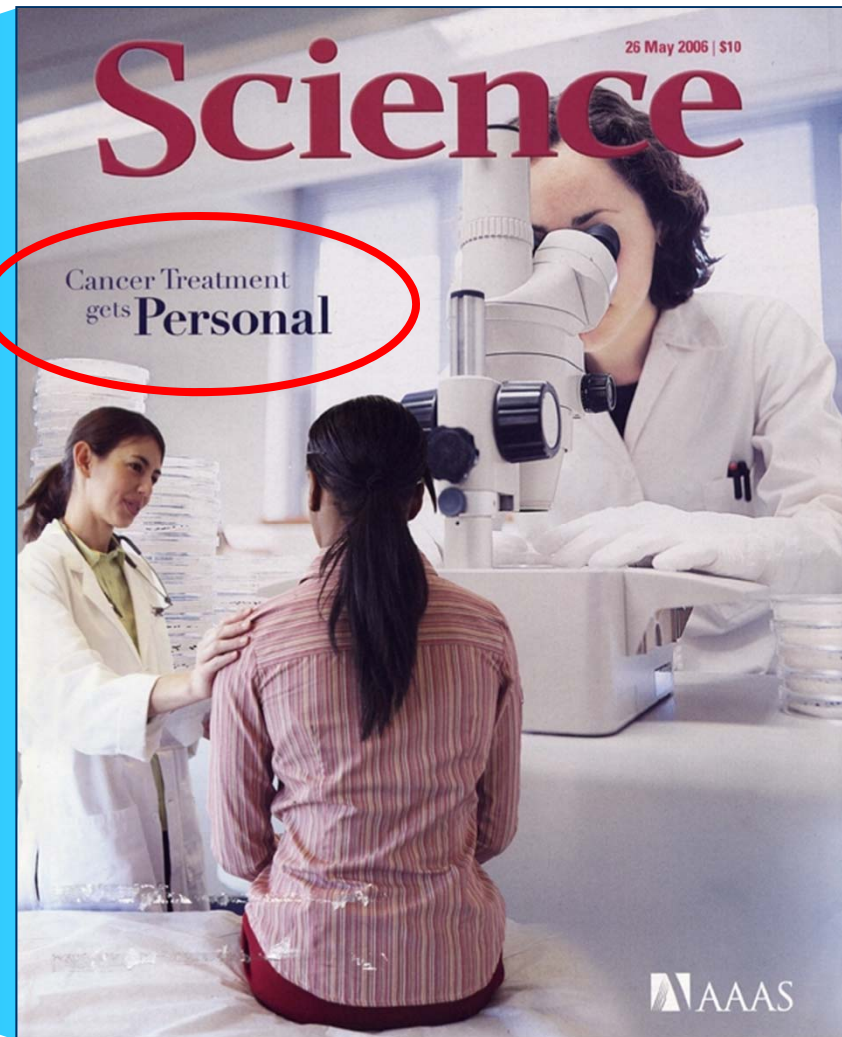


Image courtesy of Science, May 26, 2006

- **IOTF was established in 2003 to enhance the efficiency of clinical research and the scientific evaluation of new cancer treatments**

- **Examples of Key IOTF Focus Areas:**
 - **Establish joint training and fellowships**
 - **Discover and develop biomarkers for clinical benefit**
 - **Through use of caBIG™, support standardization and organization of data reporting from clinical trials, and support electronic filings to accelerate regulatory reviews**
 - **Address specific regulatory barriers impeding cancer drug development**

- Process Enhancement – Exploratory INDs for small molecules; New GMP regulations for experimental agents
- Biomarkers Qualification – **The Oncology Biomarker Qualification Initiative**
- New Common Bioinformatics Platforms – Standards for clinical trials submissions; e-INDs; CRIX Project
- Advanced Technologies – Critical Path Initiatives (nanotechnology and molecular diagnostics)
- Training and Joint Appointments – Three training programs for PhDs and MDs

- Developing biomarkers and new disease models
- Streamlining clinical trial
- Applying bioinformatics
- Enabling 21st century manufacturing
- Addressing urgent public health needs

- New **target discovery** (understand underlying biology)
- Drug **development** – markers of toxicity, metabolism, etc.
- **pharmacogenomics**
- **Early detection** (broad or specific detection / corroboration of specific disease stage)
- Identify **molecular basis of disease phenotypes**
- Assessment of disease **aggressiveness**
- **Rational** choice of **treatments** – selection for trials
- **Assessment** of treatment **effectiveness**
- **Prevention markers**

- **Technical:** Common standards are needed to evaluate biomarker technologies and compare experimental results
- **Regulatory:** Qualified biomarkers are needed as assessment tools for use in FDA guidance for cancer drug development
- **Economic:** Innovators are reluctant to conduct biomarker trials without evidence of widespread clinical applications; CMS needs evidence of clinical utility to inform reimbursement decisions
- **Structural:** Biomarker-based studies require multi-disciplinary capability (genomics, proteomics, clinical biology, engineering, image computation, biomedical informatics, trial design, etc.) *

Coordinated Effort Is Needed to Bridge the Gap Between Biomarker Discovery and Validation/Clinical Utility

* Source: Weissleder R. Molecular imaging in cancer. *Science* 312:1168-1171, 2006.

**The Oncology Biomarkers Qualification Initiative (OBQI)
is a new and innovative collaboration among
NCI, FDA, and CMS designed to qualify biomarkers for
use in clinical trials – and ultimately speed
better agents to cancer patients***



***Tri-partite MOU signed 01/23/2006**

OBQI

NATIONAL
CANCER
INSTITUTE

Develop biomarker technologies and validation protocols to improve detection, diagnosis, treatment, and prevention of cancer

FDA

Develop guidance for the use of biomarkers to facilitate cancer drug development

CMS

Make informed decisions about reimbursement of new or existing treatment regimens based on biomarker-guided knowledge

- **OBQI will validate particular biomarkers to:**
 - **evaluate new, promising technologies in a manner that will facilitate and accelerate clinical trials**
 - **reduce the time and resources spent during the drug development process**
 - **improve the linkage between drug regulatory review and drug coverage**
 - **increase the safety and improve the efficacy of drug choices for cancer patients**

- **Cancer Imaging:** Standardizing and evaluating imaging technologies
- **Molecular Assays/Targeted Therapies:** Developing scientific bases for diagnostic assays to enable personalized treatments
- **Clinical Trials:** New biomarker-driven clinical trials designs (including exploratory or “phase zero” trials)
- **Data Mining:** Pooling to share data and learning between trials

“Imaging-based biomarkers can be used in all phases of the cancer drug development process, from target discovery and validation to the pivotal clinical trials that precede drug approval.”

Ralph Weissleder; Science; May 26, 2006

- **Validated biomarker imaging data could lead to:**
 - Smaller clinical trials
 - Earlier go/no-go decisions on compounds
 - Accelerated regulatory review
 - Shorter time to public availability
 - Surrogate markers of efficacy

- **FDG-PET exploits the reliance of tumor cells on glucose and glycolytic metabolism to image cancers** (Warburg Effect, strong mechanistic rationale)
- **FDG-PET data can be assessed visually, or analyzed semi-quantitatively or quantitatively**
- **FDG-PET is approved for use in the diagnosis, staging, and restaging of a variety of cancer types, and in these applications can significantly impact the clinical management of disease**
- **In a number of clinical settings (e.g., NSCLC, esophageal cancer, lymphoma), FDG-PET can provide an early measure of response to treatment with approved therapies**
- **With a few additional studies, FDG-PET could facilitate drug development and patient care by resulting in shorter phase II trials, accelerated approval in Phase III (full approval on evidence of clinical benefit and better patient care by stopping ineffective therapies**

Note: The OBQI serves as a pilot program for a trans-NIH biomarkers initiative

- Identify mutual priorities across the three partners
- Develop scientific rationale for candidate biomarker(s)

Through the Foundation for the NIH:

- Finalize the clinical question
- Collaborative development of the protocol with community experts
- Finalize protocol
- NIH Foundation seeks partners
- Trial performance

Project 1:

FDG-PET Imaging in Non Hodgkin's Lymphoma to Predict Tumor Response to Treatment

Project 2:

FDG-PET Imaging in Non-Small Cell Lung Cancer to Predict Tumor Response to Treatment

- Successful clinical management
- Effective drugs
- Existing clinical FDG-PET data for diagnosis and staging
- Established treatment-response criteria that can be refined by FDG-PET

Objective

- Refine CR criteria with FDG-PET imaging, establish predictive value of FDG-PET after two cycles of chemotherapy
- Provide data to support FDA and CMS decision-making - based on a common understanding of the roles of these types of assessments

Clinical Trial Sites

- Approximately 20 sites will be selected, to include Comprehensive Cancer Centers
- Approximately 400 patients
- Standard chemotherapy treatment
- Imaging at baseline, and after Cycles 2 and 6 of chemotherapy

New Approach

- Multiple clinical trial sites, all following the same protocol and sharing data in real time via caBIG™

Objective

- Determine if FDG-PET scans can be used as surrogate markers of efficacy in lung cancer treatment

Clinical Trial Sites

- Approximately 15 sites will be selected, to include Comprehensive Cancer Centers
- Approximately 200 patients
- Standard, platinum-based therapy for lung cancer
- Three cycles of therapy,

New Approach

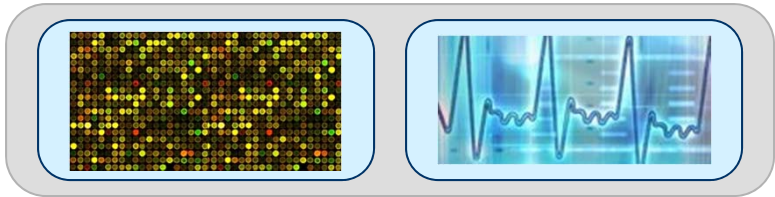
- Multiple clinical trial sites, all following the same protocol and sharing data in real time via caBIG™

- **NIH to finalize organizational structure for public-private partnership to fund biomarkers trials**
 - To be announced in Summer 2006

- **Select teams/sites for the first two OBQI trials**
 - Potential sites currently being considered and will be selected and funded in Fall 2006

- **Determine next OBQI trials**
 - Expert group to identify next trials in Fall 2006

Patient Information



Biomarker-Enabled Resources to Enhance Patient Care



- Differential diagnosis
- Optimization of therapy
- Real-time therapeutic response
- Monitoring for recurrence trial
- Clinical trials selection

Molecular, Imaging, and Clinical Knowledge

