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Workshop Report

Enhancing Drug Development and Drug Monitoring: Academia, Industry and Government Chart Common Goals

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A workshop was hosted by the Biomedical Imaging Science Initiative of the University of Southern California in January 2007, entitled "Imaging-based Tools: Role in Drug Development and Drug Monitoring". This workshop brought together leaders from the pharmaceutical and the imaging industries, from academia and from government, who worked together to identify technical, educational, financial and procedural roadblocks that have delayed progress in the pharmacokinetic imaging field. The outcome has been a report that identifies future actions, including the formation of a Multidisciplinary Advisory Council on Noninvasive Imaging Studies.

KEY WORDS: molecular imaging; noninvasive imaging; pharmacodynamics; pharmacokinetic imaging; pharmacokinetics.

"... imaging has been responsible for three of the top five greatest medical innovations of the past century and will probably continue to make major contributions to medical progress."
NIH Director, Elias Zerhouni, MD, January 2006

"Biomedical imaging in the twenty-first century offers unparalleled opportunities to transform the clinical practice of medicine and to help scientists unveil the secrets of living systems," the Academy of Radiology Research recently stated. To expedite drug development and discovery, applying proven imaging technologies may significantly accelerate time to clinical acceptance, reduce costs and improve safety. Drug imaging studies may be done either as static pictures or as a dynamic depiction of pharmacoactivity. These dynamic, or pharmacokinetic/pharmacodynamic, studies offer a dramatic portrait of the dynamics of drugs action/inaction in disease in patients, complementing more classical anatomical imaging. To fully utilize these molecular imaging technologies and others on the horizon, a number of challenges must be identified and surmounted. To proactively address these challenges, create a collaborative support network and better serve patients, a workshop was hosted by the Biomedical Imaging Science Initiative of the University of Southern California in January 2007.

The workshop, entitled "Imaging-based Tools: Role in Drug Development and Drug Monitoring," brought together leaders to work together to identify technical, educational, financial and procedural roadblocks that have delayed progress in the pharmacokinetic imaging field. Achieving the ultimate goal of pharmacokinetics—the right drug at the right dose at the right time, holds the promise to greatly reduce the economic and personal burden of patients in the treatment of many diseases.

Workshop participants were pharmaceutical scientists, imaging scientists, physicists and economists—from industry and from academia, assessed various approaches to achieving this goal. These leaders, in concert with clinicians and with representatives from the FDA and the NIH, concluded that a true collaborative effort among all stakeholders is required. Initial work is underway to review the current status and the barriers to a more comprehensive use of noninvasive imaging in the study of diagnostic and therapeutic drugs.

The recommendations that follow respond to the FDA and NCI charge to imaging stakeholders to implement the recommendations from the workshop, representative of views from academia, government and industry, that fully reflects the issues affecting imaging today, from the state of the science to current gaps to future goals. This implementation is being achieved by a Multidisciplinary Advisory Committee on Noninvasive Imaging Studies.

Detailed information on the workshop, its recommendations and links to the people developing and implementing these programs is available at the USC Biomedical Imaging Science Initiative website: http://www.usc.edu/research/initiatives/bisi/workshop/wppi/index.html

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RECOMMENDATIONS

Introduction

The goal of this workshop, held January 23 and 24, 2007, was to identify and discuss key questions regarding the development and use of dynamic, functional imaging-based tools and to propose ways for overcoming obstacles to progress in this field. Presentations were made by 23 speakers, followed by active discussion of the over 80 participants. A final session was held at the end of the meeting to summarize the key outcomes and recommendations.

One major takeaway message from the meeting is that the technology is advancing very rapidly across a number of disciplines. The rapidity of this pace presents the medical, research and drug development communities with a number of challenges and opportunities. Some of the challenges include ongoing education even within disciplines to appreciate change, focused development of new technology to solve relevant problems, finding funding in an environment where priorities change with new developments, constant recreation of new visions and directions for research, defining new regulatory measures and being open to even more technology change outside our traditional boundaries. Opportunities abound in this environment: new methods to personalize and focus treatment on specific disease sites, reduction of the healthcare cost burden, greater involvement of the medical and patient communities in diagnosis and therapy, along with the potential for faster and lower cost means to get significant research to the bedside.

Consensus

Given the diversity of the group, it is remarkable that there was a strong consensus in a number of areas, chief of which is the need for basic scientists and clinicians to interact in a truly interdisciplinary and precompetitive environment. The demands of industry and academia tend to promote interactions that delve deeply into a topic, but provide little consistent opportunity to reach across to other disciplines to investigate and solve relevant problems. Overall, there was consensus that there is a need to create, foster and institutionalize such interdisciplinary interactions, not only within a given organization, but also across to other groups and governmental agencies. How to create this cross-discipline environment and measure our success toward that goal is one starting point for discussion.

The group felt that defining commonality of goals in drug studies between academia, professional and scientific organizations, governmental agencies, the pharmaceutical industry and the imaging industry is an essential first step. Current paradigms of drug development often fail to include, if even consider, modern testing methods such as imaging and pharmacokinetic modeling. There was a broad consensus that the drug discovery/development process takes far too long and consumes too many resources to adequately address society's healthcare needs and that such needs should be addressed in a timely and cost effective manner.

Biological imaging, particularly medical imaging, has seen rapid advancement over the last few years and is now widely accepted as both a research tool and as an evaluative and predictive tool in facilitating clinical and reimbursement decisions. Pharmacokinetic/dynamic imaging is well accepted in the medical community to diagnose cancers, identify metabolic disorders and depict marginal perfusion to the brain and heart. The consensus is that these tools are not yet well integrated into our current drug development paradigms.

The need for greater support, at all levels, was a common theme. Researchers focused on imaging for PK/PD studies find it increasingly difficult to fund their work and develop new methodologies. Current priorities in the pharmaceutical and imaging industries consume most of their resources just competing in the marketplace—often funding for emerging techniques is limited. Nationally, federal agencies are often strapped with their funding to maintain the status quo while attempting to address shifting national priorities. The consensus is that more support at all levels is needed to create new medical products development paradigms.

Assuming that PK/PD imaging (PKI/PDI) continues to demonstrate positive contributions, there is a consensus that a need will exist to define some common standards: for processes/protocols, for measurements, for analysis methods and for regulatory compliance. Harmonized research protocols should allow pooling of data from multiple centers and studies. Commonly accepted and harmonized methods of measurement should similarly allow interoperable databases to be created and serve as a resource for retrospective data mining to inform future medical product development and also encourage more sharing of resources (data and biospecimens included) researchers in the process. Common methods of data analysis should allow researchers to review large databases with a consistent, high-quality toolset that would be readily acceptable to investigators and regulators. Despite some of the competitive rhetoric, the scientific and industrial communities are looking for constructive alliances where resources can be leveraged and data can be shared. Funding agencies are keenly aware that limited funds need to be allocated where they can do the greatest good. Again, there is a consensus that an accepted commonality of protocols, data acquisition and analysis are key to creating new drug development paradigms.

Pressing educational needs, and how to address them, was also a common theme. Performing imaging studies for PK/PD requires a high level of understanding of instrumentation, anatomical/physiological models, development of molecular biomarkers, pharmacologic action and quantitative interpretation tools. There is a significant shortage of educational programs in a number of key areas. The workshop consensus was that implementing PKI/PDI into the drug development regimen will require an active participation of educators, researchers, regulatory experts and others to involve the broader community, such as clinicians, industry, regulatory bodies and granting agencies.

As might be expected with any large interdisciplinary forum where major change is contemplated, there were areas where consensus was lacking.

- Who provides the support necessary to develop new paradigms
- Who performs this research (basic, technical, clinical, applied) and who owns the IP that may result
- Who changes the paradigm—corroborates findings, implements new processes and protocols
- Who validates new methods and provides QC infrastructure

• How best to develop/support cost effective drugs/biologics development with more effective approaches to PK/PD

• How do we educate ourselves and our respective communities

Each of these areas alone could require a separate workshop and working committee to create the unified vision, define the stakeholders, inventory resources available, involve broader communities and produce concrete plans for going forward. In reviewing these challenges, one point of consensus did arise—that of the creation of an institute, or institutes, where the center(s) can comprehensively work through the issues in a limited and controlled environment. Academic health centers seem the likely home to these institutes.

Recommendations

The organizers of the workshop created blocks of interactive discussion wherein aspects of PKI/PDI would be viewed with perspectives of key experts and stakeholders from the pharmaceutical and imaging industries, governmental agencies and academia. From these expert presentations and general discussions during the session, a series of the following specific recommendations were made:

1. *To foster interdisciplinary interactions*

(a) To explore how to create pre-competitive public/private partnerships, using the models provided by cooperative groups such as the Biomarker Consortium, the C-Path Institute, SAE consortium and others

(b) To stimulate focused interdisciplinary workshops aimed at addressing specific roadblocks identified at this meeting

(c) To provide incentives and rewards for imaging academicians involved in multi-disciplinary research

2. *To foster commonality of goals*

(a) To provide examples to industry of the contribution that noninvasive imaging can provide to drug development and to drug utilization studies

(b) To enhance sustained dialog between industry, academia, professional and scientific societies and regulatory agencies in order to foster the development and utilization of noninvasive imaging methods where they effectively meet the needs of science and society

(c) To work with the payer agencies (CMS, HMO and others) to identify the roadblocks limiting the introduction and adoption of innovative and new technologies and develop strategies to eliminate these roadblocks.

3. *To work with governmental and private companies to generate greater support for research and researchers focused on imaging studies for PK/PD*

(a) To identify the key areas in PK/PD imaging where support is most urgently required. Examples of key topics mentioned at the workshop included:

(i) Imaging agent development and for correlative imaging studies in therapeutic trials

(ii) Radiopharmaceutical and other tracer development for the diagnosis and monitoring of treatment of human disease in clinical practice and research trials

(iii) High sensitivity, high specificity imaging probes with the goal toward clinical applications

(iv) Computational models based on systems approaches

(b) To work with the NIH, other funding agencies and industry to generate support for such areas

4. *To develop and make available harmonized methods of measurement and data analysis*

(a) To foster and harmonize the development of imaging phantoms suitable for quantitative multi-modality imaging

(b) To foster the development of harmonized methods of data acquisition in CT, MRI, PET/SPECT and Optical working in partnership with the instrument manufacturers. (NEMA).

(c) To foster the development of open source informatics tools for analyzing imaging data.

5. *To provide education in imaging studies for PK/PD*

The first step in the implementation of this process is to identify the existing scientific and health gaps, evaluate what is available, both in order to avoid unnecessary duplication as well as to reinforce, if appropriate, existing efforts. This is to be followed by proposals to be developed aimed at exploring:

(a) The development of short courses, 1–3 days in duration, to be offered at either academic, professional societies or work sites

(b) The development of on-line courses in noninvasive imaging studies at various levels

(c) The possibility of longer programs, individually or in groups, that would provide an in-depth education and training on noninvasive imaging principles and methods

(d) The incorporation of functional imaging methods into residency programs in various medical specialties

(e) The development of graduate and post-doctoral programs in functional/dynamic noninvasive imaging studies

Future Actions

In order to implement these recommendations a Multidisciplinary Advisory Council for Noninvasive Imaging Studies (MACNIS) has been formed, whose mission is to develop further the above consensus ideas and recommendations from the workshop. The Biomedical Imaging Science Initiative at USC has agreed to initiate and facilitate this Council. Please contact Prof. Walter Wolf (wwolfw@usc.edu) for further information.