QIBA Steering Committee Conference-Call Meeting

Thursday, June 18, 2020
10:00 am – 11:30 am (CT)

Draft Summary

In attendance:

Daniel Sullivan, MD (Chair)
Alex Guimaraes, MD, PhD (Co-chair)
Timothy Hall, PhD (Co-chair)
Michael Boss, PhD
Andrew Buckler, MS
Paul Carson, PhD
Caroline Chung, MD
Patricia Cole, PhD, MD
Therese Cooper, BS, RDMS
Renee Cruea, MPA
Nandita deSouza, MD
J. Brian Fowlkes, PhD
Brian Garra, MD
Rudresh Jarecha, MBBS
Paul Kinahan, PhD
Emily Lacey, MS
P. David Mozley, MD
James Mulshine, MD
Nancy Obuchowski, PhD
Kevin O'Donnell, MASc
Mark Rosen, MD, PhD
Annette Schmid, PhD
Lawrence Schwartz, MD
Lalitha Shankar, MD, PhD
Anne Smith, PhD
Gudrun Zahlmann, PhD
Brian Zimmerman, PhD

Guest Speakers:
Suzanne George, MD
Jacob Hesterman, PhD
Ronald Korn, MD, PhD
Paul McCracken, PhD
Peter O'Dwyer, MD
Theresa Tuthill, PhD

Guests:
Michael Knopp, MD, PhD
Etta Pisano, MD

RSNA Staff:
Angela Colmone, PhD
Fiona Miller
Joe Koudelik
Tori Peoples

Dr. Sullivan welcomed SC members and guest panelists to the call. A brief tribute to the late Dr. Edward Jackson, past QIBA Chair, was presented highlighting his numerous achievements in medical physics, the radiologic sciences, and his warm and caring personal character.

Pharmaceutical company perspective (late stage, e.g., oncology): Patricia Cole, PhD, MD (Bayer US)

Dr. Cole noted the various Profile benefits to drug development and oncology; of particular focus was metastatic disease. She noted that Biomarkers (BMs) also need to be optimized for decision making.

In summary:

- CT Volumetry was very useful in measuring change in liver lesions
- FDG-PET is useful but lacks surrogate endpoints for phase 3 trials (limited clinical applications)
- DWI useful for assessing cell death in early and late phase trials
    - Expanding to whole body suggested
- Zirconium labeled antibodies need standardization for industry
- DCE (v1.0) was useful for early phase drug development, but somewhat outdated today
- SPECT (Tc99m) shows promise, but less impact than PET in drug development

She indicated that industry recognizes the value of a standardized protocol library (e.g., UPICT), and QIBA Profiles define a needed level of imaging performance. Dr. Cole noted the importance of Phase 1 and 2 BMs and the need to address the severe condition of most patients re: number of visits and their lower tolerance for scans/imaging.

Of additional interest to Pharma:

- Gallium tracers
- 18-F PET
- PSMA tracers
- Immune cell imaging BMs / immuno-oncology / radiotherapeutics and gene therapies
- Radiomics/genomics for drug development

Pharmaceutical company perspective (early stage, e.g., dose finding): Theresa Tuthill, PhD (Pfizer)

Dr. Tuthill presented the big Pharma perspective and growing interest in the Non-Alcoholic Steatohepatitis (NASH) liver studies. Different aspects of fatty liver disease need to be quantified. State of the art of current NASH trials was presented. The imaging focus on three histological pillars of NASH was presented (fat, inflammation, fibrosis). Reader variability and liver inhomogeneity are challenges. Dr. Tuthill reinforced the need for a non-invasive, comprehensive assessment of NASH. Imaging BM's are being used as a primary endpoint in a phase 2 study, replacing biopsy. Accuracy (based on phantoms), analysis tools, and overall standardization is needed world-wide.

Significant Profiles for drug development include:

- DWI
- MRE
- DCE v1.0
- US SWS for comparison with MRE performance
- PDFF for assessing dose response
- PEQUS

Imaging CRO perspective (late stage): Paul McCracken, PhD (ICON)

Dr. McCracken noted the ongoing discussion with sponsors regarding the transformative power of BMs to increase clinical trial success by using imaging endpoints. Many sponsors remain hesitant regarding BMs in drug development since this deviates from the typical, time-honored process used since the 1950's. Sponsors need better convincing as to the absolute value of imaging in clinical trials. Unfortunately, good marketing often beats out good science today. The concept of cost effectiveness needs better advocacy, e.g., fewer patients and shorter time for trials. Validation of QIBA methods based on clear, robust measurable quantitative endpoints are needed to engage industry.

Dr. McCracken noted that he routinely references QIBA Profiles in discussions with sponsors.

Significant Profiles for ICON include:

- CT Vol and FDG-PET already used in trials
- MRE Profiles for the liver need to advance
- F-18, Amyloid and Tau BMs are needed
- PDFF for liver fat can be an endpoint in phase 2 trials for decision making
- ASL of high value
- Machine learning (ML) needs QIBA standardization and validation of methods
- Standardization and accessibility to BMs is critical
- Radiomics field growing fast – more opportunity here to standardize
    - QIBA focuses on metrics based on ground truth, it is not clear if Radiomics and ML fall under this paradigm since ground truth is often unknown

Imaging CRO perspective (early stage): Jacob Hesterman, PhD (Invicro, LLC)

Dr. Hesterman noted that neuro and immuno-oncology tracers are of primary interest to Invicro, which has its own imaging center in the UK. Invicro is also an early adopter of QIBA conformance; their London imaging site has worked through the QIBA self-attestation (SA) process and has attained conformance with the DWI Profile. The current field of tracers needs standardization and quantitation. Standardization also needed for software packages and analysis tools.

Although QIBA conformance can be rigorous, in-depth, and time-consuming, these processes are still doable. A balance of practicality vs. accuracy is possible in a clinical trial setting. QIBA and UPICT materials have proven to be excellent references to follow.

Significant Profiles for Invicro include:

- DWI whole body for early stage drug development
- Amyloid
- FDG-PET
- SPECT I-123 beneficial for early and late stage treatment
- SPECT Tc99m

New areas of interest include:

- PSMA PET – more prevalent in early and late phase trials
- MR Volumetrics – the neuro analytics side needs help
- AI/Radiomics
- Dosimetry quantitation growing for new tracer evaluation in early stage trials
- Historical data – steps in pre-processing to increase data consistency to aid in downstream analysis and reproducibility

Imaging CRO perspective (late stage): Ronald Korn, MD, PhD (Imaging Endpoints)

Dr. Korn noted the CRO role as an essential fulcrum in imaging today. CROs need to improve imaging quality and accuracy. Being a practicing radiologist, and teaching residents, Dr. Korn sees the practical

and clinical side of this initiative. Both rigorous science and practicality need to be integrated for clinical trials. Since 50-60% of new drugs go to registration, the field needs to be prepared that imaging can be part of the approval process and must be done correctly. QIBA's role here is to provide imaging standardization to produce better data. This must start with scanner harmonization to compare output results (Dr. Sunderland's work in PET is essential here). Standardization for response assessment needed since pharma is already basing optimal dose recommendations on imaging results.

The RECIST Committee needs to recognize the QIBA standard as key reference for clinical sites. BMs are very useful and standardization across various tracers is critical. PET technology is advancing fast; we need to integrate high and low technology for FDA approval.

Areas of interest to Imaging Endpoints:

- FDG-PET
- Radiomics
- Theragnostics - How to translate diagnostic scans to theragnostics of interest?
- COVID-19 – The landscape is changing today; perhaps a Profile (with ACR approval) to help manage image quality would be useful

NCI Cooperative Group Perspective (early stage): Peter O'Dwyer, MD (ECOG/ACRIN)

Dr. O'Dwyer provided an overview of his role with the cooperative groups. With the help of Drs. Rosen and Mankoff at U Penn, BMs were integrated at an early stage of drug development. Medicine needs well validated BMs for their predictive power, proof of mechanism, pharmacokinetic qualities, tumor heterogeneity, drug targeting and toxicity.

He noted there is a large disconnect between the imaging sciences and the clinical trial field: "we don't know what we don't know." He suggested QIBA could help demonstrate the possibilities and limitations of quantitation, and the Cooperative Groups are a ready audience. Oncologists rely on imaging to assess tumors that are refractory to immuno-oncology drugs. Microenvironment and metabolic imaging are also areas of interest that are potential targets for QIBA assistance. BMs to assess the full tumor (structure) quantitatively are needed.

Dr. O'Dwyer indicated radiomics is a topic of interest across all Cooperative Groups but lacks standardization. ECOG/ACRIN could help to address standardization but better education of stakeholders regarding the value of QIBA is critical.

NCI Cooperative Group Perspective (late stage): Suzanne George, MD (Alliance)

Dr. George provided an overview of the National Clinical Trials Network (NCTN) organizational structure. With a centralized function, NCTN serves numerous groups, such as ECOG/ACRIN, SWOG and the Alliance. Staffed by 10,000 cancer specialists across 600 hospitals in the US and Canada, NCTN oversees studies ranging from phase 1-3, with the bulk being 2-3. All groups may interface with the Imaging

Response Oncology Center (IROC) in different ways. Approximately 1,000 community practices make up the bulk of the NCTN structure.

Sites are located across the US, including academic, community, urban and rural centers. The challenge is to match the research question to the proper environment, i.e., which member sites have the proper tools to participate in a new trial. Goal for imaging biomarkers is to develop something new, with minimal added burden to sites and staff, and needs to be feasible to implement at sites. Dr. George noted that pilot studies at specialized centers were also implemented. BMs were deemed critical to drug development for Gastrointestinal Stromal Tumors (GIST), e.g., PET used in the early development of tyrosine kinase inhibitors (of GIST) demonstrating clear evidence of response. There is much NCI can learn from QIBA.

General comments from guests:

Dr. Etta Pisano noted that QIBA Profiles may be difficult to implement in busy clinical practices, especially if phantom scanning is required for QA. Patient accrual may be hindered if more demands are placed on busy clinics.

Dr. Lawrence Schwartz reiterated the need to focus on pilot studies at specialized imaging centers. These high-performing sites are easily identified, will accept the additional (process) burden, e.g., phantom scanning, to obtain better results … more effort and funding/support would be expected.

Dr. Michael Knopp noted that many opportunities exist to bring specialty BMs into the NCTN via various pathways, e.g., BMs could be seen as exploratory trial components. Funding support is always useful to improve data generation and processing.

To integrate the QIBA process into the NCTN imaging standard of care remains the challenge. Dr. Knopp suggested examining "points of variability" between the current (imaging) standard of care and QIBA to support the added value of QIBA processes but the required test/retest studies are a hurdle in large trials and would require support, e.g., grants such as R01, U01, etc.

Dr. Lalitha Shankar noted that ACRIN is funded by NCI, and flexibility does exist to ask PI's to utilize QIBA Profiles, but that challenges can be encountered in getting trial teams to agree. Integrating BMs within imaging in treatment trials often results in pushback. Assessments from pilot studies at 2-3 centers would be helpful to make the case to oncologists that QIBA tools are ready to be tested in a multi-center program.

Dr. Sullivan thanked all SC members and guest presenters for their valued time and input.

Next QIBA Steering Committee T-con: September 17th at 10 am – 11:30 am (CT)
Proposed agenda topic: What is the QIBA value proposition for hardware and software vendors?