Molecular Imaging – Advancing Drug Development from Preclinical Studies to Global Multicenter Trials

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Bi-Directional Translational Molecular Imaging

Use of Imaging Biomarkers in Drug Development
- As a surrogate endpoints
  - e.g., a biomarker that is intended to substitute for a clinical endpoint
  - Tumor shrinkage (RECIST criteria)
  - Can be used in Phase III as a primary endpoint
  - Pharmacodynamics
- Prognostic biomarkers
  - Used prior to treatment to predict negative and positive results
  - Patient stratification
    - Hypoxic status of tumor
    - Hormone receptor expression
- Predictive Biomarkers
  - Used to assess effect of drug treatment
    - Early metabolic response with FDG-PET in lymphoma and solid tumors
    - Early anti-proliferative effects with FLT-PET
    - Receptor occupancy for dose guidance and schedule

Qualification with clinical outcome

Biomarker: FDG-PET SUVmax
Patient Population: GIST
Therapeutic: Tyrosine Kinase Inhibitor

Holdsworth et al. AJR 2007

Mantle Cell Lymphoma FLT-PET: CDK 4/6 Inhibitor
Demonstration of Specific Target Hit

Prediction of clinical outcome

Need for Standardized Imaging and Clinical Trials Network

- High-quality well designed clinical trials with imaging biomarkers are essential
  - To provide data for approval of new radiopharmaceuticals
  - To accelerate the approval of new therapeutics
  - Demonstrate efficacy in the clinical management of disease
- Standardized imaging methodology is essential in multicenter trials
  - To minimize the variance in measurements
  - Account for differences in scanners and sites
  - Detect real treatment effects in small numbers of patients
- The current published studies are often inadequate to support CMS and national guidelines decisions

CTN Achievements

- Database and reporting tool (DaRT) developed and on-line
- FLT IND approved; 4 DMF letters of cross-reference
- Completed one site qualification demonstration project (Siemens; 10 sites, 12 scanners)
- Currently assisting with 6 trials (2 under CTN FLT IND, 4 FDG)
- Developed educational curriculum for both technologists and physicians. Courses offer CE credits
- Collaboration with NCCN for scanner validation
- Equipment manufacturers group working on image reconstruction harmonization for multicenter trials

CTN Validated PET/CT Scanners and Qualified Imaging Sites

171 PET/CT scanners
122 sites
FDG USA Clinical Production Sites

106 sites

18FDG Worldwide Production Sites

122 sites

18FLT Worldwide Production Sites

64 sites: 52 USA
12 sites in 8 other countries

 Booth #433

www.snm.org/clinicaltrials