Application for QIBA Project Funding

Title of Proposal: Analysis of SARC 11 Trial PET Data by PERCIST with Linkage to Clinical Outcomes		
QIBA Committee/Subgroup: FDG PET Technical Committee		
NIBIB Task Number(s) which this project addresses: 10		
Project Coordinator or Lead Investigator Information:		
Last Name: Wahl	First Name: Richard	Degree(s): MD
Institution/Company: Johns Hopkins University School of Medicine		

Please check the primary category for this proposal from among the following:

☐ 1. Identification of Technical Characteristics and Standards

- ☐ a. Creation and refinement of protocols for image acquisition, analysis, quality control, etc., for specific clinical utility
- ☐ b. Phantom development and testing
- ☐ c. Identification and assessment of intra-reader bias (1) and variance across scanners and centers
- ☐ d. Identification and assessment of inter-reader bias and variance across scanners and centers
- ☐ e. Other

X ☐ 2. Clinical Performance Groundwork

- ☐ a. Assessment of intra-reader sensitivity and specificity
- ☐ b. Assessment of inter-reader sensitivity and specificity

X ☐ c. Other

☐ 3. Clinical Efficacy Groundwork

- ☐ a. Assessment of correlation between new biomarker and 'accepted-as-standard' method

X ☐ b. Characterization of value in clinical trials

- ☐ c. Characterization of value in clinical practice

X ☐ d. Development/merger of databases from trials in support of qualification

- ☐ e. Other

X ☐ 4. Resources (money and/or people) committeed from other sources.

All PET scans were acquired and paid for by the Sarcoma Alliance for Collaboration as part of the SARC 11 trial. All therapeutic drugs and clinical follow up to determine survival, PFS and response were paid for by the SARC 11 trial. All necessary computers for analysis are in place and provided by the JHU IRAT laboratory and the division of nuclear medicine at JHU.

Please provide a one-page summary that includes the following information:

Project Description:

The insulin-like growth factor (IGF) pathway plays an important role in a variety of physiological processes in humans and animals, including normal growth and development. Additionally, this pathway has been shown to play an important role in the development of conditions like cancer. IGF signaling has been proposed to play a major role in the very aggressive nature of certain sarcomas, like Ewing's sarcoma family of tumors (ESFT) and synovial sarcomas

The SARC 11 trial prospectively evaluated the utility of an anti Insulin like Growth Factor Human Monoclonal Antibody (R1507) as monotherapy for Sarcomas of several types (Recurrent or Refractory Ewing's Sarcoma, Osteosarcoma, Synovial Sarcoma, Rhabdomyosarcoma and Other Sarcomas.) . All patients received R1507 9mg/kg i.v. . This single arm study evaluated the efficacy and safety of **R1507** in patients with recurrent or refractory sarcoma Clinical efficacy of the trials was judged by: Objective response rate [Time Frame: Week 24, and every 12 weeks thereafter] , Progression-free survival in patients with Ewing's sarcoma [Time Frame: Week 18] , Duration of response, PFS, and overall survival.

In this multicenter study, a baseline PET scan was obtained as well as a PET scan at approximately 9 days post therapy initiation. A follow up scan at 12-18 weeks was obtained in those remaining on study. A total of 311 patients entered the study. Importantly, the PET was not used to alter the therapy. Thus, the PET data can be used to determine prognostic ability. Accrual to the study is now complete and the full PET data set have been collected and are available in DICOM form for analysis. Details of the SARC 11 trial and the rationale for anti IGF antibody therapy are detailed at Clinical Trials. gov and the SARC website.

http://www.clinicaltrials.gov/ct2/show/related/NCT00642941?term=r1507 and http://www.sarctrials.org/SARC011r1507

We propose to analyze the PET data quantitatively (and qualitatively) using PERCIST and EORTC response criteria to determine how predictive PET, notably changes in PET signal between baseline and the first follow up scan, is of clinical outcomes. We will also examine inter-observer consistency. We will apply commercial software and our in house developed software for analysis. This trial is particularly suitable for analysis of PET data as they are not biased by management alterations from the PET results, a key and essential element to evaluating a potential biomarker.

Primary goals and objectives:

To analyze quantitatively and qualitatively the FDG PET data prospectively obtained at up to three time points in the SARC 11 trial (311 patients accrued). The analyses will focus on linkage of PET findings to clinical outcomes of response, PFS and survival. Specific metrics to be assessed include:

a) PERCIST criteria response
b) EORTC criteria response
c) Analysis using glycolytic volumes (TLG and TV)
d) Qualitative assessments of response by three readers
e) Linkage of these values to clinical outcomes

Deliverables:

a) Transfer of image data set to JHU IRAT servers
b) Quality analysis of PET data for compliance with PERCIST standards
c) Normal tissue quality assessments
d) Visual analysis of PET data
e) Quantitative analysis of PET data
f) Linkage of results to clinical outcomes
g) Manuscript (s) of results for publication and support of FDA qualification

These include linkage of PET changes in SUV to response

Timeline [must include intermediate measureable milestones.]

Months 0-3: Transfer of data sets to JHU and assessment of quality
Months 3-6: Visual analysis of PET data
Months 6-10: Quantitative assessment of PET data
Months 10-12: Statistical analysis of data including linkage to outcomes and preparation of final reports. Includes precision analysis of both the Visual and Quantitative data assessed by the 3 readers.